

failure to provide an enabling disclosure. First, the Examiner contends that the disclosure is not enabling because "[i]t is not evident that the deposited biological materials mentioned in the claims are permanently available to the public."

Applicant encloses herewith copies of the December 13, 1991 Declaration of James F. Haley, Jr. (**Exhibit A**) and the June 3, 1994 Supplemental Declaration of James F. Haley, Jr. (**Exhibit B**). Those declarations demonstrate that applicant has converted the microorganisms referred to as G-pBR322(Pst)/HFIF3 (DSM 1791), G-pBR322(Pst)/HFIF6 (DSM 1792), and G-pBR322(Pst)/HFIF7 (DSM 1793) to deposits under the Budapest Treaty, and has averred that the deposits will be maintained for the enforceable life of the patent and that all restrictions on availability to the public will be irrevocably removed upon granting of the patent.

Microorganism G-pBR322(Pst)/HFIF1, which was not deposited, harbors a plasmid encoding the HFIF1 (IFN- β) DNA insert. As shown in Fig. 5, the HFIF1 DNA insert is a 680 base pair subset of the larger HFIF3, HFIF6 and HFIF7 DNA inserts, each of which is carried on a plasmid in one of the microorganisms deposited under the provisions of the Budapest Treaty and referred to in the declarations of James F. Haley, Jr. Because the HFIF1 insert may be derived directly from any one of the three plasmids harbored by deposited microorganisms, a G-pBR322(Pst)/ HFIF1 microorganism deposit is not essential to enable one of skill in the art to produce the claimed HFIF1 DNA insert using the information disclosed in the specification as filed.

Second, the Examiner contends that the disclosure is non-enabling because it fails to teach "what amounts of human

IFN- β 1 may or may not be effective in a therapeutic method of tumor treatment in humans." Applicant respectfully traverses.

First, the application as filed teaches an appropriate starting concentration range from which the skilled practitioner (i.e., physician or oncologist) can empirically determine an optimized treatment program on an individual basis. The specification states:

[i]nterferon therapy against ... tumors or cancers has been conducted at varying dosage regimes and under several modes of administration.... It is usually administered one to three times daily in dosages of 10^4 to 10^7 units.... [T]umors and cancers are usually treated by daily or multiple daily doses over several months or years. The most effective therapy for a given patient must of course be determined by the attending physician, who will consider such well known factors as the course of the disease, previous therapy and the patient's response to interferon in selecting a mode of administration and a dosage regime.

Specification, page 4, lines 11-30.

Second, several studies published before the effective filing date of this application used native human IFN- β to treat tumor cells in culture or tumors in vivo. For example, Einhorn and Strander, J. Gen. Virol., 35, pp. 573-77 (1977) (copy enclosed as **Exhibit C**) (referred to at specification page 5, lines 18-22), showed that purified native IFN- β inhibited osteosarcoma cell growth in vitro at concentrations of 10 and 100 units/ml (p. 574). Horoszewicz et al., Cancer Treat. Rep., 62, pp. 1899-1906 (1978) (copy enclosed as **Exhibit D**), showed that purified native IFN- β injected directly into human metastatic lesions (malignant melanomas of about 5 mm diameter) at a concentration of 5×10^5 units (U) per day for 14 days was extremely effective in reducing tumor size and eliminating tumor cells (p. 1902). Nemoto et al., Amer. Assoc. For Cancer Res., Abs. No. 993, p. 246 (1979) (copy enclosed as **Exhibit E**) (referred to at specification page 6, line 35 - page 7, line 1), reported that daily injections for 30 consecutive days of 0.5 or

1.0 x 10⁶ U of purified native IFN- β into subcutaneous nodules of melanoma and breast carcinoma patients (3 patients each) resulted in strong local tumor regression in all but one melanoma patient.

The relative concentrations of purified native IFN- β reported to be effective in inhibiting human tumor cell growth in publications such as those referred to above could be used in combination with applicant's disclosure by the skilled practitioner as a guide for determining an appropriate recombinant IFN- β dosage schedule for a particular tumor type in a particular patient. Accordingly, the application as filed, in view of the state of the art at the effective filing date, would have enabled one of skill in the art to initiate a therapeutic anti-tumor treatment program using the method recited in applicant's claims.

For all of these reasons, applicant respectfully requests that the Section 112, first paragraph, rejections be withdrawn.

THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

The Examiner contends that claims 31 and 32 are indefinite and vague for reciting the phrase "substantially free of other proteins with which it is normally associated" in the absence of disclosure about which proteins IFN- β normally associates with. Applicant has cancelled claim 32 and has deleted the phrase "substantially free of other proteins with which it is normally associated" from amended claim 31, thus obviating this rejection.

The Examiner also objects to the phrases "characterized by" and "characterized in that," recited in claims 31 and 32, respectively. Those phrases have been deleted from

applicant's amended claims. Claim 32 has been cancelled and amended claim 31 recites "a recombinant DNA molecule comprising a DNA sequence."

Applicant's amended claims are no longer indefinite and, accordingly, applicant requests that the Section 112, second paragraph, rejections be withdrawn.

THE REJECTIONS UNDER 35 U.S.C. § 103

A. The Taniguchi/Roberts/Borden Combination

The Examiner has rejected claims 31, 33 and 34 under 35 U.S.C. § 103 as "unpatentable" over Taniguchi et al., Gene, 10, pp. 11-15 (1980) ("Taniguchi") in view of Roberts, Proc. Natl. Acad. Sci. USA, 76, pp. 5596-600 (1979) ("Roberts") and further in view of Borden et al., Annals of Internal Med., 91, pp. 472-79 (1979) ("Borden"). The Examiner contends that it would have been obvious for one of skill in the art at the time the invention was made to express the human IFN- β 1 gene of Taniguchi using methods disclosed in Roberts to produce large amounts of IFN- β 1 for anti-tumor therapy as suggested by Borden. Applicant traverses this rejection based on the specific facts of this case as well as the law, as described in detail below.

The success of the Examiner's rejection requires first, that the combination of Taniguchi and Roberts be proper, and second, that the combination disclose or suggest the human IFN- β polypeptide recited in applicant's amended claims. Neither one of these requirements is met here.

1. The Combination Of Taniguchi And Roberts Is Improper

There is no basis for the Examiner's combination of Taniguchi and Roberts. Neither document teaches or suggests the combination: Taniguchi says nothing about expression and

Roberts says nothing about expressing an interferon, much less human IFN- β . Neither suggests resolving the difference between the prior art and the claimed invention. In re Vaeck, 947 F.2d 488 (Fed.Cir. 1991) (reversing obviousness determination because "the prior art in this case offers no suggestion, explicit or implicit, of the substitution that is the difference between the claimed invention and the prior art.")

In addition, the Examiner has presented no evidence supporting his purported combination. Ex parte Levengood, 28 USPQ2d 1300, 1301 (Bd.Pat.App.Intf. 1993) ("it is necessary for the examiner to present evidence ... that one having ordinary skill in the art would have been led to combine the relevant teachings of the applied references in the proposed manner to arrive at the claimed invention.") The only evidence here is to the opposite -- the ordinarily skilled artisan at the effective filing date of this application would not have made the Taniguchi/Roberts combination.

First, the IFN- β gene of Taniguchi was a "copy DNA" (cDNA) on a bacterial plasmid (pBR322) unlinked to any plasmid expression control sequences. Because cDNA is enzymatically copied messenger RNA (mRNA), which starts downstream from the major expression control sequences of the gene (e.g., promoter and enhancer elements), the human IFN- β cDNA of Taniguchi was also not linked to any endogenous expression control sequences. The Examiner does not disagree that expression or even capability for expression was missing from Taniguchi. Instead, the Examiner contends that it would have been obvious for the skilled practitioner to express Taniguchi's IFN- β cDNA using the system of Roberts. This contention, however, is unwarranted for several reasons.

Roberts disclosed a bacterial plasmid in which the simian virus SV40 small tumor ("t") antigen gene was fused precisely to transcription and translation control sequences of the E. coli lac operon to create a "hybrid ribosome-binding site." Roberts, Abstract, lines 7-11. Bacteria transformed with such constructs were screened for SV40 expression products using antibody-containing serum from animals harboring SV40-induced tumors. SV40-related immunoreactive polypeptides were then characterized. Roberts concluded that in order to express the t antigen, a fairly precise juxtaposition between the ATG of the SV40 t gene and the lac operon Shine-Delgarno (SD) (translation control) sequences was required:

"synthesis is barely detectable if the distance between the lac SD sequence and the ATG of t is large (17 base pairs).... support[ing] the notion that formation of a hybrid ribosome-binding site bearing appropriately positioned SD and ATG sequences is essential to translation of t."

Roberts, p. 5600, Discussion, first paragraph (emphasis added).

Significantly (and a point that the Examiner ignores), Roberts did not teach or suggest that this protocol would be successful for expressing any other eukaryotic gene in bacteria. In the words of Roberts, their experiment provided a "rational approach [not a solution] to the problem of obtaining expression of eukaryotic genes in bacteria." Roberts, p. 5600, Discussion, last sentence.

Nor did Roberts teach or suggest that the human IFN- β cDNA of Taniguchi could be fused to the lac operon of E. coli, with the same distance constraints and in the same manner as the SV40 t gene was to successfully express a human IFN- β polypeptide in bacteria.

Roberts also did not show that the SV40 t polypeptides expressed from their lac fusion constructs possessed any biological activity. The t polypeptides were detected based

only on their ability to bind to SV40-specific antibodies. Thus Roberts failed to teach or suggest that their method could be used to express and isolate a biologically active, SV40 t antigen, let alone a biologically active human IFN- β , in bacteria or in any other host. Yet, applicant's claims require that the IFN- β be biologically active because otherwise it will not be useful in the claimed methods.

In addition, the Roberts approach could not and did not address the specific problems inherent in the expression of IFN- β . For this reason, the ordinarily skilled artisan would not have selected the Roberts approach in attempts to express IFN- β . Applicant submits herewith copies of the Declaration of Richard L. Cate (hereinafter referred to as "Cate Decl. ¶ ___") (Exhibit F), and the Supplemental Declaration of Richard L. Cate (hereinafter referred to as "Cate Supp. Decl. ¶ ___") (Exhibit G), both filed in co-pending application Serial No. 08/471,646, which describe the problems inherent in recombinantly expressing IFN- β . Cate Supp. Decl. ¶ 26.

Therefore, under the law and the facts, the Examiner's combination (even if it was proper to make, which it was not) fails to render the claimed invention unpatentable. "All the evidence on the question of obviousness must be considered." In re Piasecki, 745 F.2d 1468, 1471 (Fed.Cir. 1984). This includes the marked differences between SV40 t antigen and IFN- β . Because of these differences, there is simply no basis for selecting the Roberts approach over any other possible approach known in 1980. Cate Supp. Decl., ¶ 26.

There is also contemporaneous proof that the Taniguchi/Roberts combination is improper. None of the workers in 1980, including Dr. Ptashne, Dr. Roberts himself (who best knew the Roberts approach), and Dr. Taniguchi, used the Roberts

approach in their attempts to express IFN- β -- they chose not to make the combination that the Examiner is making in hindsight some 15 years later. Cate Decl. ¶ 62. Instead, they used a new method (i.e., that of Guarente). Cate Decl. ¶ 62. Dr. Goeddel also did not use the Roberts approach. Cate Decl. ¶ 62.

This contemporaneous attitude towards the "Roberts approach" is powerful evidence of non-obviousness. See Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 1143 (Fed.Cir. 1985). See also Ex parte Goeddel, Appeal No. 94-2099 (August 31, 1994) at 8 (copy enclosed as Exhibit H) (stating "we have attempted to place ourselves 'back in time' when the invention was made").

2. There Was No Reasonable Expectation Of Success

There was also no reasonable expectation of success in attempts to produce recombinant IFN- β in 1980 before applicant achieved it for the first time.

Dr. Cate's declarations detail the expected problems in the recombinant production of IFN- β and explain why these problems did not provide the ordinarily skilled artisan with a reasonable expectation of success. Cate Decl. ¶¶ 9-17, 22-35, 39-44, 46, 52, 61, 65; Cate Supp. Decl. ¶¶ 3-4. To emphasize the point, Dr. Cate expressly stated that expression of recombinant IFN- β was "unpredictable." Cate Decl. ¶ 11; Cate Supp. Decl. ¶ 4.

Applicant summarizes below why there was no reasonable expectation of success.

First, Roberts was a "general approach". That is insufficient. A general approach amounts only to an "obvious-to-try" situation -- a standard for obviousness that has been repeatedly rejected. Gillette Co. v. S.C. Johnson & Son, Inc.,

919 F.2d 720, 725 (Fed.Cir. 1990) ("An 'obvious-to-try situation' exists when a general disclosure may pique the scientist's interest ...").

Further, Roberts does not solve any of the specific or general problems confronting one of skill in the art trying to express IFN- β . As described above, Roberts neither taught nor suggested that the specific sequence and distance constraints found necessary for producing SV40 t antigen polypeptides from lac-SV40 t gene fusions would be effective generally for expressing any eukaryotic gene. To the contrary, Roberts expressly acknowledges that heterologous gene expression was a "problem". See Roberts, p. 5600; Cate Decl. ¶ 54; Cate Supp. Decl. ¶ 26.

Taniguchi (as well as other prior art) identified the unique properties of IFN- β . Based on these properties, the ordinarily skilled artisan would have expected problems in the recombinant production of IFN- β . These included problems with proteolytic degradation, bioinactivity, toxicity, and insolubility. Cate Supp. Decl. ¶¶ 7-8. Specific problems due to IFN- β 's three cysteine (Cys) residues and extreme hydrophobicity were also expected. Cate Supp. Decl. ¶¶ 9-23. There was no reasonable expectation of success in overcoming those problems. Cate Supp. Decl. ¶¶ 23, 27-28. See also decision of the Board of Appeals and Patent Interferences, Goeddel v. Weissmann, Interference 101,601, Paper No. 265 (December 15, 1995) ("Goeddel v. Weissmann Decision") (copy enclosed as Exhibit I) at 24-26.

Further, in 1980 the ordinarily skilled artisan could not have ruled out the possibility that IFN- β underwent post-translational processing during expression and secretion. This would have been a concern because of the discrepancy between the

molecular weight of IFN- β as measured with the native glycosylated protein and that predicted from the sequence reported in Taniguchi. Cate Decl. ¶ 22. See also Fantes, p. 177 (Cate Supp. Decl., Exhibit 20).

In 1980, the ordinarily skilled artisan could not have predicted that such post-translational processing would occur correctly (or at all) in a heterologous host. For this reason too, then, there was no reasonable expectation of success in attempts to produce recombinant IFN- β . This is supported by the Board in Ex parte Goeddel (*supra*), which stated that one skilled in the art in 1980 would not have been able to predict whether non-glycosylated IFN- β (one class of applicant's non-human interferons) would be biologically active. As a consequence, they also could not predict that such interferon could be used in the methods of claims 31 and 33-34.

Perhaps, the best evidence that on June 6, 1980, one of ordinary skill in the art would not have had a reasonable expectation of success using Roberts to express IFN- β is what the skilled workers actually did at the time. They did not use the Roberts approach. Dr. Roberts and Dr. Taniguchi did not use the Roberts approach when they collaborated to express recombinant IFN- β -- after applicant. This fact is persuasive contemporaneous evidence that those who knew the Roberts approach best did not believe that it provided a reasonable expectation of success. See Interconnect Planning, 774 F.2d at 1143 (stating "[a] retrospective view of the invention is best gleaned from those who were there at the time"). Instead, they used a new method referred to in Guarente, published after applicant's June 6, 1980 priority date. Guarente expressly states that identification of expressing transformants using the

Roberts approach "may be laborious or impossible." Guarente, p. 544; Cate Decl. ¶ 62.

Dr. Goeddel also subsequently expressed IFN- β . He too did not use the Roberts approach. Cate Decl. ¶ 62.

Furthermore, Dr. Taniguchi and Dr. Roberts thought that expression of IFN- β was patentable. They filed a patent application claiming that subject matter. EP-A 0 042 246; Cate Decl. ¶ 63. So did Dr. Goeddel. EP-A 0 048 970; Cate Decl. ¶ 63. And, the Board has held Goeddel's expression of a subgenus of IFN- β -- microbially produced, mature, non-glycosylated IFN- β -- to be patentable in September 1980 -- three months after applicant expressed IFN- β the first time. See United States patent 5,460,811 ("the '811 patent") (enclosed as Exhibit J) (cited in the Supplemental Information Disclosure Statement filed concurrently herewith), which was allowed over both Roberts and Taniguchi, cited here. See also the '811 patent, p. 1, column 2, line 26 and p. 2, column 1, lines 16-17.

The foregoing demonstrates that there was no reasonable expectation of success in attempts to produce recombinant IFN- β at applicant's June 6, 1980 priority date.

The Examiner's rejection is also totally inconsistent with two recent decisions of the Board of Appeals and Patent Interferences: (1) Goeddel v. Weissmann, *supra*; and (2) Ex parte Goeddel, *supra*.

Those decisions by two different panels: (1) APJs R. Smith, Downey and W. Smith (Goeddel v. Weissmann); and (2) APJs Winters, W. Smith and Gron (Ex parte Goeddel); specifically address the same issue that underlies the Examiner's Section 103 rejection: with the DNA sequence for an interferon in hand, would it have been obvious to the skilled person to express that DNA and produce biologically active interferon in April 1980 and

in September 1980 (two months before and three months after applicant's June 6, 1980 latest priority date here). Resoundingly, both Boards said NO. Fundamental fairness requires a consistent application of that law here.

Goeddel v. Weissmann

This interference concerned the expression of mature IFN- α in April 1980. The Count was to the mature polypeptide itself (Decision, p.3):

"A polypeptide of about 165-166 amino acids comprising the amino acid sequence of a mature human leukocyte interferon microbially produced and unaccompanied by any corresponding presequence or portion thereof."

In April 1980, the DNA sequence encoding mature IFN- α was known and available (Decision, p. 18). In April 1980, the sequence of the mature IFN- α was also known (Decision, p. 19). This art, thus, stands in the same position and provides the same information as Taniguchi cited here by the Examiner. Roberts, the second document cited by the Examiner here, was certainly prior art in April 1980.* Yet, the Board held that the expression of the polypeptide of the Count was not enabled (Decision, pp. 24-32). See in particular, Decision, p. 24:

"As is clear from the April '80 EPO application, as of April 1980, the ability of workers to express human proteins in bacteria was a very recent advance in molecular biology, i.e., the field was in its infancy";

Decision, p. 31:

"While those individual steps and techniques may have been known at that time, in view of the embryonic nature of this field and the lack of guidance in the specification [just like in Roberts here], it is difficult to find a reasonable basis to conclude that one would have obtained expression of the protein by these techniques without further guidance as to the direction that experimentation should take";

* A variety of prior art Goeddel documents that described expression generally and the expression mature hGH and other mature proteins stood in the place of Roberts in the interference (Decision, p. 21).

and Decision p. 32:

"Boyer stated that 'every protein had its own series of problems relating to expression'."

Incredibly, the Board reached its finding of non-enablement notwithstanding a fact that is not present here -- in April 1980, Weissmann had already expressed immature IFN- α in E. coli and shown that it was biologically active. This Board disregarded that fact (applicant's assignee believes improperly). It held that the expression of immature interferon was irrelevant to the issue at hand -- it was a compound outside of the Count (Decision, p. 32). How much more so is the Roberts' expression of a non-interferon protein (the SV40 t antigen) irrelevant to the expression of IFN- β . On the basis of this decision alone, therefore, the Examiner should withdraw his Section 103 rejection.

Ex parte Goeddel

The second Board decision -- Ex parte Goeddel -- only confirms the inappropriateness of the Examiner's Section 103 rejection here. The claim at issue in Ex parte Goeddel was a composition comprising a non-glycosylated mature human fibroblast interferon, i.e., IFN- β (Decision p. 2):

"25. A composition comprising water and a nonglycosylated polypeptide having the amino acid sequence of a mature human fibroblast interferon, said nonglycosylated polypeptide having a total of 165 or 166 amino acids and said composition being free of any glycosylated human fibroblast interferon."

The cited prior art included Taniguchi (cited here) and the Goeddel Nature article which was relied on in Goeddel v. Weissmann as showing the expression of mature hGH and other proteins (i.e., analogous to Roberts here). The time frame was

even later than the June 6, 1980 priority date here. The Goeddel application was filed on September 25, 1980.

Much like the rejection here, the rejection in Ex parte Goeddel was under Section 103 (Decision p. 6):

"[T]he examiner argues [in view of Taniguchi and Goeddel] that a person having ordinary skill would have been motivated to produce appellants' nonglycosylated polypeptide using recombinant expression in E. coli because of the known benefits of such a procedure (greater yields, faster production, ability to obtain high purity)'".

The Board reversed (Decision, p. 8). It held (Decision, p. 6):

"With respect to each prior art rejection, the examiner's position presupposes that the hypothetical person having ordinary skill in this art would have reasonably expected appellants' nonglycosylated polypeptide to possess biological activity. This is not the case".

The same logic must apply here. Applicant's polypeptide is produced in a non-human host, and as such, it is not identical to known IFN- β . Its biological activity, thus, is unpredictable.

For all the reasons discussed above, the combination of Taniguchi and Roberts is both an improper one and one which had no expectation of success to those of skill in the art at the effective filing date of this invention. Accordingly, the portion of the Examiner's Section 103 rejection based on the Taniguchi/Roberts/Borden combination should be withdrawn.

B. The Knight/Borden Combination

The Examiner has rejected claims 32-34 under 35 U.S.C. § 103 as "unpatentable" over Knight et al., Science, 207, pp. 525-26 (1980) ("Knight"), in view of Borden et al., Annals of Internal Med., 91, pp. 472-79 (1979) ("Borden"). The Examiner contends that it would have been obvious for one of skill in the

art at the time the invention was made to isolate human IFN- β 1 in the manner of Knight and to use it for anti-tumor therapy as suggested by Borden. Applicant has obviated this rejection by cancelling claim 32. Amended claims 33 and 34 depend only from amended claim 31.

For these reasons, the amended claims are not obvious over the cited art. Accordingly, applicant requests that the Examiner withdraw the 103 rejections.

CONCLUSION

For all of the above reasons, reconsideration and allowance of the pending claims is requested.

Respectfully submitted,

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Examiner : J. Martinell
Group : 1805
Applicant : Walter C. Fiers
Serial No.: 387,503
Filed : July 28, 1989
For : DNA SEQUENCES, RECOMBINANT DNA MOLECULES AND
PROCESSES FOR PRODUCING HUMAN FIBROBLAST
INTERFERON-LIKE POLYPEPTIDES

08/452658

New York, New York
December 13, 1991

Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

DECLARATION OF JAMES F. HALEY, JR.

I, JAMES F. HALEY, JR., declare that:

1. I am the attorney of record in the above-identified patent application. I make this declaration to set forth the facts related to the deposit of microorganisms referred to on pages 94-95 of that application and to the permanence, availability and replacement of those cultures.

2. I identify the following documents that demonstrate the deposit of those microorganisms and the permanence, availability and replacement of those cultures:

Exhibit 1 -- True copies of seven Deutsche Sammlung von Mikroorganismen "Acknowledgement of Receipt and Acceptance" for cultures HFIF-A through HFIF-G (DSM 1791-1793 and 1851-1854). The acknowledgments confirm that these deposits were made on April 2, 1980 and June 5, 1980, respectively, under Title 37, Code of Federal Regulations, and the other applicable rules and regulations of the United States Patent and Trademark Office.

Exhibit 2 -- True copies of a February 27, 1981 letter to me from the American Type Culture Collection and

Consent
10/11/96
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Exhibit 3 -- True copies of an October 16, 1991 letter from me to the Deutsche Sammlung von Mikroorganismen with enclosures including seven Deutsche Sammlung von Mikroorganismen applications to convert into a deposit under the Budapest Treaty the deposit of a microorganism already deposited outside the Budapest Treaty for cultures HFIF-A through HFIF-G (DSM 1791-1793 and 1851-1854).

Exhibit 4 -- True copies of a October 16, 1991 letter from me from the American Type Culture Collection with enclosures including two requests to convert a deposit to meet the requirements of the Budapest Treaty for the cultures HFIF-H and HFIF-I (ATCC 31824 and 31825).

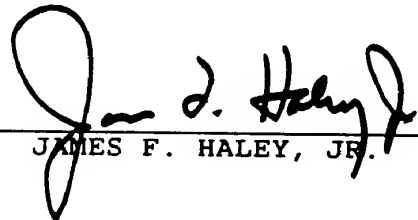
Exhibit 5 -- A true copy of a Budapest Treaty Receipt Of Request And Viability Statement from ATCC confirming that the deposits for cultures HFIF-H and HFIF-I (ATCC 31824 and 31825) have been converted to Budapest treaty deposits.

Exhibit 6 -- True copies of Budapest Treaty Receipt Of Request And Viability Statements from Deutsche Sammlung von Mikroorganismen confirming that the deposits for cultures HFIF-A through HFIF-G (DSM 1791-1793 and 1851-1854) have been converted to Budapest treaty deposits.

3. On the bases of the above-identified exhibits, I am informed and believe that the deposits of microorganisms referred to on pages 94-95 of the above-identified application were made, have been converted to deposits under the Budapest Treaty On The International Recognition Of The Deposit Of Microorganisms For The Purposes Of Patent Procedure and are being maintained under the applicable rules and regulations of that Treaty and of

agrees to maintain the permanence of these deposits for the full enforceable term of any patent issuing from this application and to irrevocably remove all restrictions on the availability to the public of the material so deposited upon the granting of a patent in accordance with the requirements of 37 C.F.R. §§ 1.806 and 1.808.

5. The undersigned declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.


JAMES F. HALEY, JR.

Signed at New York, New York
this 13'th day of December, 1991.

I Hereby certify that this correspondence is being deposited with the U. S. Postal Service as First Class Mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231, on

Dec. 13, 1991

CORA L. SCOTT
Name of Person Signing


Signature of Person Signing

ACKNOWLEDGEMENT OF RECEIPT AND ACCEPTANCE

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikroorganismen.

Name and address of depositor: Biogen N.V.
24 Handelskad
Willemsted
Curacao, Netherland Antilles

Identification reference of the microorganism used by the depositor: HFIF-A
HB101(G-pBR322(Pst))/HFIF 3)

Taxonomic designation of the microorganism provided by the depositor: Escherichia coli

DSM accession number of the microorganism: DSM 1791

Date of receipt of the viable microorganism: April 2, 1980

In addition to the identification reference and the taxonomic designation the depositor has ~~provided~~ ^{XXX} / has not provided a scientific description of the microorganism.

- ☒ The microorganism has been sent to the DSM directly by the depositor.
- ☐ The microorganism has been sent to the DSM on behalf of the depositor by the following depository under the designation and accession number given:

As stated by the depositor the microorganism may be rendered accessible to any third party under the following conditions:

- ☐ without any restrictions
- ☒ according to Rule 28 EPC and to the agreement between the European Patent Organisation and the DSM (Official Journal EPO 5, 301-307, 1978) and/or
- ☒ according to the Swedish patent legislation and to the agreement between the Swedish Patent Office and the DSM (Svensk Patenttidning nr 12, 1979)
- ☒ in accordance with the "Declaration of Release" to be filed by the depositor with the DSM and the German Patent Office (at present Form P 2570)
- ☒ in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14) and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of America and b) without any restriction on availability to the public of the culture upon granting of a United States patent wherein the deposited microorganism is part of the disclosure of the invention
- ☒ in accordance with the French patent law
- ☐ in accordance with the conditions as specified by the depositor on enclosed separate sheet.

Göttingen, April 2, 1980

Place date DEUTSCHE SAMMLUNG VON MIKROORGANISMEN
Signature
der
Gesellschaft für Biotechnologische Forschung mbH
Gneibachstraße 8
D-3400 Göttingen

Gesellschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig, Tel.: (05 31) 70 08-1, Telex: 9-5 26 67

Vorsitzender des Aufsichtsrats: Herr Dr. Dr. Friedrich Bischoff	Geschäftsführer: Dr. Maria Regina Kula Dr. Heimit Zeithäger	Bankkonto: Gebr. Löffbecke, Braunschweig Konto 23 761 (BLZ 25 0 5 5 0)	Registergericht: Amtsgericht Braunschweig HRB 477
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003-0979

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikroorganismen.

Name and address
of depositor:

Biogen N.V.
24 Handelskad
Willemsted
Curacao, Netherland Antilles

Identification reference of
the microorganism used by
the depositor:

HFIF-B
HB101(G-pBR322(Pst)/HFIF 6)

Taxonomic designation of
the microorganism provi-
ded by the depositor:

Escherichia coli

DSM accession number of
the microorganism:

DSM 1792

Date of receipt of the
viable microorganism:

April 2, 1980

In addition to the identification reference and the taxonomic designation the depositor ~~XXXX~~ ~~XXXXXX~~ has not provided a scientific description of the microorganism.

- ☒ The microorganism has been sent to the DSM directly by the depositor.
☐ The microorganism has been sent to the DSM on behalf of the depositor by the following depository under the designation and accession number given:

As stated by the depositor the microorganism may be rendered accessible to any third party under the following conditions:

- ☐ without any restrictions
☒ according to Rule 28 EPC and to the agreement between the European Patent Organisation and the DSM (Official Journal EPO 5, 301-307, 1978) and/or
☒ according to the Swedish patent legislation and to the agreement between the Swedish Patent Office and the DSM (Svensk Patenttidning nr 12, 1979)
☒ in accordance with the "Declaration of Release" to be filed by the depositor with the DSM and the German Patent Office (at present Form P 2570)
☒ in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14) and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of America and b) without any restriction on availability to the public of the culture upon granting of a United States patent wherein the deposited microorganism is part of the disclosure of the invention
☒ in accordance with the French patent law
☐ in accordance with the conditions as specified by the depositor on enclosed separate sheet.

Göttingen, April 2, 1980

Place date DEUTSCHE SAMMLUNG VON MIKROORGANISMEN
Signature
der
Gesellschaft für Biotechnologische Forschung mbH
Grisebachstraße 8
D-3400 Göttingen

Gesellschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig, Tel.: (05 31) 70 08-1, Telex: 9-5 26 67

Vorsitzender des Aufsichtsrats:
Min. Dir. Dr. Friedrich Bischoff

Geschäftsführer:
Dr. Maria Regina Kula
Dr. Helmut Zenträger

Bankkonto:
Gebr. Löbbecke, Braunschweig
Konto 23 781 (BLZ 270 305 00)

Registriergericht:
Amtsgericht Braunschweig
HRB 477

ACKNOWLEDGEMENT OF RECEIPT AND ACCEPTANCE

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikroorganismen.

Name and address
of depositor:

Biogen N.V.
24 Handelskad
Willemsted
Curacao, Netherland Antilles

Identification reference of
the microorganism used by
the depositor:

HFIF-C
HB101(G-pBR322(Pst))/HFIF 7)

Taxonomic designation of
the microorganism provi-
ded by the depositor:

Escherichia coli

DSM accession number of
the microorganism:

DSM 1793

Date of receipt of the
viable microorganism:

April 2, 1980

In addition to the identification reference and the taxonomic designation the depositor has provided / has not provided a scientific description of the microorganism. ^{XXX}

- ☒ The microorganism has been sent to the DSM directly by the depositor.
☐ The microorganism has been sent to the DSM on behalf of the depositor by the following depository under the designation and accession number given:

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☒ in accordance with the "Declaration of Release" to be filed by the depositor with the DSM and the German Patent Office (at present Form P 2570)
☒ in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14) and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of America and b) without any restriction on availability to the public of the culture upon granting of a United States patent wherein the deposited microorganism is part of the disclosure of the invention
☒ in accordance with the French patent law
☐ in accordance with the conditions as specified by the depositor on enclosed separate sheet.

Göttingen, April 2, 1980

Place

date

DEUTSCHE SAMMLUNG VON MIKROORGANISMEN
der

Gesellschaft für Biotechnologische Forschung mbH
Grisebachstraße 8

D-3400 Göttingen

Gesellschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig. Tel.: (05 31) 70 08-1, Telex: 9-5 26 67

Vorsitzender des Aufsichtsrats:
Min. Dir. Dr. Friedrich Bischoff

Geschäftsführer:
Dr. Maria Regina Kula
Dr. Helmut Zeitträger

Bankkonto:
Gebr. Löbbecke, Braunschweig
Konto 23 781 (BLZ 270 305 00)

Registergericht:
Amtsgericht Braunschweig
HRB 477

003-0979

ACKNOWLEDGEMENT OF RECEIPT AND ACCEPTANCE

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikroorganismen.

Name and address
of depositor:

BIOGEN N.V.
24 Handelskad
Willemsted,
Curacao, Netherland Antilles

Identification reference of
the microorganism used by
the depositor:

HFIF-D
M5219 (G-pLa-HFIF-67-12)

Taxonomic designation of
the microorganism provi-
ded by the depositor:

Escherichia coli

DSM accession number of
the microorganism:

DSM 1851

Date of receipt of the
viable microorganism:

June 5, 1980

In addition to the identification reference and the taxonomic designation the depositor ~~has~~
~~XXXXXX~~ / has not provided a scientific description of the microorganism.

- ☒ The microorganism has been sent to the DSM directly by the depositor.
☐ The microorganism has been sent to the DSM on behalf of the depositor by the following
depository under the designation and accession number given:

As stated by the depositor the microorganism may be rendered accessible to any third party
under the following conditions:

- ☐ without any restrictions
☒ according to Rule 28 EPC and to the agreement between the European Patent Organisation
and the DSM (Official Journal EPO 5, 301-307, 1978) and/or
☒ according to the Swedish patent legislation and to the agreement between the Swedish
Patent Office and the DSM (Svensk Patenttidning nr 12, 1979)
☒ in accordance with the "Declaration of Release" to be filed by the depositor with the
DSM and the German Patent Office (at present Form P 2570)
in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14)
and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of
☒ America and b) without any restriction on availability to the public of the culture
upon granting of a United States patent wherein the deposited microorganism is part
of the disclosure of the invention
☒ in accordance with the French patent law
☐ in accordance with the conditions as specified by the depositor on enclosed separate
sheet.

Göttingen, June 5, 1980

Place

date

DEUTSCHE SAMMLUNG VON MIKROORGANISMEN

der

Signature

Gesellschaft für Biotechnologische Forschung mbH

Grisebachstraße 8

D-3400 Göttingen

Gesellschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig, Tel.: (05 31) 70 08-1, Telex: 9-5 25 67

Vorsitzender des Aufsichtsrats:
Min. Dir. Dr. Friedrich Bischoff

Geschäftsführer:
Dr. Maria-Regina Kula
Dr. Helmut Zeitträger

Bankkonto:
Gebr. Löffbecke, Braunschweig
Konto 23 781 (BLZ 270 305 00)

Registergericht:
Amtsgericht Braunschweig
HRB 477

003-3979

ACKNOWLEDGEMENT OF RECEIPT AND ACCEPTANCE

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikroorganismen.

Name and address
of depositor:

BIOGEN N.V.
24 Handelskad
Willemsted,
Curacao, Netherland Antilles
HFIF-E
K12ΔHI (G-pPLa-HFIF-67-12)

Identification reference of
the microorganism used by
the depositor:

Taxonomic designation of
the microorganism provi-
ded by the depositor:

Escherichia coli

DSM accession number of
the microorganism:

DSM 1852

Date of receipt of the
viable microorganism:

June 5, 1980

In addition to the identification reference and the taxonomic designation the depositor ^{XXX}
~~has~~ / has not provided a scientific description of the microorganism.

- ☒ The microorganism has been sent to the DSM directly by the depositor.
☐ The microorganism has been sent to the DSM on behalf of the depositor by the following
depository under the designation and accession number given:

As stated by the depositor the microorganism may be rendered accessible to any third party
under the following conditions:

- ☐ without any restrictions
☒ according to Rule 28 EPC and to the agreement between the European Patent Organisation
and the DSM (Official Journal EPO 2, 301-307, 1978) and/or
☒ according to the Swedish patent legislation and to the agreement between the Swedish
Patent Office and the DSM (Svensk Patenttidning nr 12, 1979)
☒ in accordance with the "Declaration of Release" to be filed by the depositor with the
DSM and the German Patent Office (at present Form P 2570)
☒ in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14)
and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of
America and b) without any restriction on availability to the public of the culture
upon granting of a United States patent wherein the deposited microorganism is part
of the disclosure of the invention
☒ in accordance with the French patent law
☐ in accordance with the conditions as specified by the depositor on enclosed separate
sheet.

Göttingen, June 5, 1980

Place

date

DEUTSCHE SAMMLUNG VON MIKROORGANISMEN

der

Signature

Gesellschaft für Biotechnologische Forschung mbH

Grisebachstraße 8

D-3400 Göttingen

Gesellschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig. Tel.: (05 31) 70 08-1, Telex: 9-5 28 67

Vorsitzender des Aufsichtsrats:
Min. Dir. Dr. Friedrich Bischoff

Geschäftsführer:
Dr. Marra-Regina Kula
Dr. Helmut Zeitträger

Bankkonto:
Gebr. Löffbecke, Braunschweig
Konto 23 781 (BLZ 270 305 00)

Registergericht:
Amtsgericht Braunschweig
HRB 477

ACKNOWLEDGEMENT OF RECEIPT AND ACCEPTANCE

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikroorganismen.

Name and address
of depositor:

BIOGEN N.V.
24 Handelskad
Willemsted,
Curacao, Netherland Antilles

Identification reference of
the microorganism used by
the depositor:

HFIF-F
M5219 (G-pPLa -HFIF-67-12Δ19)

Taxonomic designation of
the microorganism provi-
ded by the depositor:

Escherichia coli

DSM accession number of
the microorganism:

DSM 1853

Date of receipt of the
viable microorganism:

June 5, 1980

In addition to the identification reference and the taxonomic designation the depositor ~~has~~
provided / has not provided a scientific description of the microorganism.

- ☒ The microorganism has been sent to the DSM directly by the depositor.
☐ The microorganism has been sent to the DSM on behalf of the depositor by the following
depository under the designation and accession number given:

As stated by the depositor the microorganism may be rendered accessible to any third party
under the following conditions:

- ☐ without any restrictions
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and the DSM (Official Journal EPD 5, 301-307, 1978) and/or
☒ according to the Swedish patent legislation and to the agreement between the Swedish
Patent Office and the DSM (Svensk Patenttidning nr 12, 1979)
☒ in accordance with the "Declaration of Release" to be filed by the depositor with the
DSM and the German Patent Office (at present Form P 2570)
in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14)
and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of
☒ America and b) without any restriction on availability to the public of the culture
upon granting of a United States patent wherein the deposited microorganism is part
of the disclosure of the invention
☒ in accordance with the French patent law
☐ in accordance with the conditions as specified by the depositor on enclosed separate
sheet.

Göttingen, June 5, 1980

Place

date

DEUTSCHE SAMMLUNG VON MIKROORGANISMEN

der

Gesellschaft für Biotechnologische Forschung mbH
Grisebachstraße 8

D-3400 Göttingen

D. Ober

Signature

Gesellschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig, Tel.: (05 31) 70 08-1, Telex: 9-5 26 87

Vorsitzender des Aufsichtsrats:
Min. Dir. Dr. Friedrich Bischoff

Geschäftsführer:
Dr. Maria-Regina Kula
Dr. Helmut Zeitträger

Bankkonto:
Gebr. Löffbecke, Braunschweig
Konto 23 781 (BLZ 270 305 00)

Registergericht:
Amtsgericht Braunschweig
HRB 477

ACKNOWLEDGEMENT OF RECEIPT AND ACCEPTANCE

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikroorganismen.

Name and address
of depositor:

BIOGEN N.V.
24 Handelskad
Willemsted,
Curacao, Netherland Antilles

Identification reference of
the microorganism used by
the depositor:

HFIF-G
M5219 (G-pPlc-HFIF-67-8)

Taxonomic designation of
the microorganism provi-
ded by the depositor:

Escherichia coli

DSM accession number of
the microorganism:

DSM 1854

Date of receipt of the
viable microorganism:

June 5, 1980

In addition to the identification reference and the taxonomic designation the depositor ~~has~~
~~XXXXXX~~ / has not provided a scientific description of the microorganism.

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☐ The microorganism has been sent to the DSM on behalf of the depositor by the following
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☒ according to the Swedish patent legislation and to the agreement between the Swedish
Patent Office and the DSM (Svensk Patenttidning nr 12, 1979)
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DSM and the German Patent Office (at present Form P 2570)
in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14)
and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of
☒ America and b) without any restriction on availability to the public of the culture
upon granting of a United States patent wherein the deposited microorganism is part
of the disclosure of the invention
☒ in accordance with the French patent law
☐ in accordance with the conditions as specified by the depositor on enclosed separate
sheet.

Göttingen, June 5, 1980

Place

date

DEUTSCHE SAMMLUNG VON MIKROORGANISMEN

der

Signature

Gesellschaft für Biotechnologische Forschung mbH
Grisebachstraße 8

D-3400 Göttingen

Gesellschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig, Tel.: (05 31) 70 08-1, Telex: 9-5 26 67

Vorsitzender des Aufsichtsrats:
Min. Dir. Dr. Friedrich Bischoff

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Dr. Maria-Regina Kula
Dr. Helmut Zeitträger

Bankkonto:
Gebr. Löffbecke, Braunschweig
Konto 23 781 (BLZ 270 305 00)

Registergericht:
Amtsgericht Braunschweig
HRB 477

003-0979

AMERICAN TYPE CULTURE COLLECTION

• 301-881-2600
12301 PARKLAWN DRIVE
ROCKVILLE, MARYLAND 20852

February 27, 1981

James F. Haley, Jr., Esq.
Attorney for Biogen N.V.
c/o Fish & Neave
277 Park Avenue
New York, New York 10172

Gentlemen:

We received on February 26, 1981 a deposit of cultures of organisms identified as Escherichia coli M5219(G-pLa-HFIF-67-124MI), HFIF-H, and Escherichia coli HB101(p[325]-qHFIF-4), HFIF-I.

These strains have been assigned the ATCC numbers 31824 and 31825, respectively.

We understand that these organisms are being deposited in the American Type Culture Collection (ATCC) in connection with the filing of an application for a patent.

We further understand that the deposit of these cultures does not grant to ATCC during the effective term of the patent anticipated a license, either expressed or implied to infringe the patent, and our release of these cultures to others does not grant them a license, either expressed or implied, to infringe the patent.

We further understand that if these cultures should die or be destroyed during the effective life of the patent it shall be your responsibility to replace them with living cultures of the same organisms.

We agree in consideration for a one-time service charge, not to distribute these cultures or any information relating thereto or to their deposits until such time as a patent has been issued disclosing the above deposits except in accordance with a U.S. Patent Office Rule of Practice, Rule 14, or until you authorize us to make these strains available. After a patent is issued and we are so informed the cultures will be made available for distribution to the public. The ATCC agrees to maintain the cultures for a period of 30 years from the deposit date. Non-payment of the service charge within 90 days of the deposit date relieves the ATCC from the above provisions.

Payment in the amount of \$1,140.00
received. Thank you.

Sincerely yours,



By: (Mrs.) Bobbie A. Brandon

An independent non-profit organization incorporated in Washington, D. C. and devoted to the preservation of reference cultures and their distribution to the scientific community

1. Scientific name of organism E. coli M5219(G-OTa-HFE-67-12AMT)
2. Strain designations other than ATCC number HFIF-H
3. Is this the type strain of this organism (see reverse side)? No
4. If this strain has been designated in the literature as the type strain, please cite reference:

Do not write in this box	
ATCC #	<u>318211-</u>
Accession date	<u>2/26/81</u>
Date received	<u>2/26/81</u>

5. Name and address of depositor: Biogen N.V.
15 Pietermaai
Curacao, Netherlands Antilles

6. Isolated by _____
from _____ date _____

7. If you did not isolate this strain, indicate from whom you received it:

ATCC ← depositor ←

8. Reason for deposit:

Requested by ATCC _____

New taxon: Species _____ Subspecies _____

Produces the antibiotic _____

Assay of _____

Production of _____

Other Patent

9. Maintenance:

Medium (attach formula) LB Broth or bactotryptone

Temperature 28°C Other LB Broth supplemented with 50 µg/ml Kanamycin

10. a) Does this organism survive: Freeze drying? Yes Freezing? Yes (poorly)

b) Recommended method for long-term preservation:

Freeze drying or LB Broth/glycerol or DMSO at -80°C

11. Is this strain zoopathogenic? No If so, would you classify it as class 2, 3, or 4? _____
(see reverse side for description of classes)

12. Is this strain phytopathogenic? No (Information required by Plant Quarantine Division, USDA)

If so, a) Is the geographical distribution of this organism general, limited, or unknown (encircle)?

b) Would you recommend that this strain be made available to any qualified investigator regardless of his location? _____

c) If not, what limits would you place on the distribution of this strain?

13. Please attach a complete description of this strain unless description is given in accompanying reprint.

14. References (Please enclose two (2) of each pertinent reprint, if available):

15. Comments:

Do not heat above 28°C.

ATCC Form 1-B (1971)

J. J. H. H. H.
Signature of Depositor
Attorney for Biogen N.V.

1. Scientific name of organism E. coli HB101 (D[325]-gHFIF-4)
 2. Strain designations other than ATCC number HFIF-I
 3. Is this the type strain of this organism (see reverse side)? No
 4. If this strain has been designated in the literature as the type strain, please cite reference:

Do not write in this box	
ATCC #	<u>31825</u>
Accession date	<u>2/26/81</u>
Date received	<u>2/24/81</u>

5. Name and address of depositor: Biogen N.V.
15 Pietermaai
Curacao, Netherlands Antilles
6. Isolated by _____
 from _____ date _____
7. If you did not isolate this strain, indicate from whom you received it: _____
 ATCC ← depositor ← _____
8. Reason for deposit:
 Requested by ATCC _____
 New taxon: Species _____ Subspecies _____
 Produces the antibiotic _____ Assay of _____
 Production of _____ Other Patent
9. Maintenance:
 Medium (attach formula) LB Broth or bactotryptone
 Temperature _____ other LB Broth supplemented with 100 µg/ml carbeniclin and/or 10 µg/ml tetracycline.
10. a) Does this organism survive: Freeze drying? Yes Freezing? Yes (poorly)
 b) Recommended method for long-term preservation:
Freeze drying or LB Broth/glycerol or DMSO at -80°C
11. Is this strain zoopathogenic? NO If so, would you classify it as class 2, 3, or 4? _____
 (see reverse side for description of classes)
12. Is this strain phytopathogenic? NO (Information required by Plant Quarantine Division, USDA)
 If so, a) Is the geographical distribution of this organism general, limited, or unknown (encircle)?
 b) Would you recommend that this strain be made available to any qualified investigator regardless of his location? _____
 c) If not, what limits would you place on the distribution of this strain?
13. Please attach a complete description of this strain unless description is given in accompanying reprint.
14. References (Please enclose two (2) of each pertinent reprint, if available):
15. Comments:

J. D. Halsey Jr.
 Signature of Depositor
 Attorney for Biogen N.V.

ROBERT C. MORGAN
KENNETH S. MERRMAN
EDWARD F. MULLOWNEY
ROBERT R. JACKSON
JESSE J. JENNER
W. EDWARD BAILEY
DAVID J. LEE
PATRICIA A. MARTONE
KEVIN J. CULLIGAN
GLENN A. OUSTERHOUT
SUSAN PROGOFF
MARGARETA PIERRE
RON E. SHULMAN
DOUGLAS J. DILBERT
DENISE L. LORING
JEFFREY H. INGERMAN

TELECOPIER: (212) 715-0674

October 16, 1991

FREDERICK P. FISH
1855-1930
CHARLES NEAVE
1867-1937

DAVID C. PLACHE
JANE A. MASSARO
DUANE-DAVID HOUDIN
MITCHELL P. BROOK
JOHN F. WARD
EDWARD J. DEFRANCO
HAROLD ROWLAND
PHILIPPE Y. RIESEN
MARK D. ENGELMANN
ERIC R. HUSSARD
DAVID A. LOEWENSTEIN
JOHN J. CASSINGHAM
LINDA A. WADLER
KELSEY I. NIX
MARTAE GROSS
JOHN H. HINTZ
JOHN R. STORELLA
WILLIAM J. MCCABE
JOHN M. DESMARAIS
VICKI S. VEENKER
LESLIE A. McDONELL
CHRISTOPHER P. DODZIELA
NICHOLAS PISANO
DONALD K. REEDY
GABRIELLE E. HIDDINS
JENNIFER M. HALL
DONALD L. RHODES
ELIZABETH M. ALORIO
CLAYS WILSON
BRENDA J. PANICHI
JEREMY LACK
EVAN H. GSELL
JAMES P. SERGIN
RONALD A. KRASNOW
JEFFREY H. HERSH
LIANNAC KALMAR
BRADFORD L. FRIEDMAN
DEBRA A. SONTOMO
LORETTA A. HIRAGLIA
MOREYS WILDES
CHRISTOPHER J. HARNETT
MARIE H. MACNICHOL
WILLIAM A. SCHONEMAN

Mrs. Bobbie Brandon
American Type Culture Collection
12301 Parklawn Drive
Rockville, MD 20852

Biogen - B8/B8 CIP
Deposits identified as ATCC 31824 and ATCC 31825

Dear Mrs. Brandon:

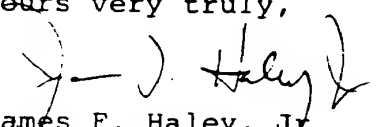
We have enclosed two (2) requests for conversion of the above-identified deposits to meet the requirements of the Budapest Treaty. The ATCC designations, as well as the strain designations given by the depositor, are identified on the request forms. In addition, we enclose copies of the letter of receipt of these deposits and of the original deposit applications containing the media and culture requirements.

Please note that the original depositor has undergone a corporate name and address change, from Biogen N.V., 15 Pietermaai, Curacao, Netherlands Antilles, to Biogen, Inc., 14 Cambridge Center, Cambridge, Massachusetts, U.S.A. 02142. This name and address change has been duly registered according to the national laws in the Patent Office of each country where a patent application has been filed referencing these deposits.

If you have any questions or require further information, please do not hesitate to contact us.

Thanks for your help.

Yours very truly,


James F. Haley, Jr.
Ivor R. Elrifi
Attorneys for Biogen, Inc.

JFH/IRE:bb
Enclosures

**TO DEPOSIT OR TO CONVERT A DEPOSIT TO MEET THE REQUIREMENTS OF
BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE
DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE**

- *1. Name of deposit (microorganism, cell, seed, plasmid, etc.) Escherichia coli
HB101 (p[325]-qHFIF-4)
2. Strain designation given by the depositor (number, symbols, etc.) HFIF-I
3. Is this an original deposit under the Budapest Treaty? _____
4. Is this a request for a conversion of a deposit already at the ATCC to meet the requirements of the Budapest Treaty? (If so, indicate ATCC designation.) Yes, ATCC 31825
5. Is this deposit a mixture of microorganisms or cells? NO
6. Details and conditions necessary for the cultivation of the strain, for its storage and for testing its viability and also, where a mixture of microorganisms is deposited, descriptions of the components of the mixture and at least one of the methods permitting the checking of their presence.
see attached sheets
7. An indication of the properties of the strain which are or may be dangerous to health or the environment, or an indication that the depositor is not aware of such properties. Depositor is not aware of any
properties of the strain which are or may be dangerous to health or
the environment.
- *8. It is recommended that sufficient description be provided to allow the ATCC to confirm that the strain deposited generally conforms to that which the depositor states is being deposited (i.e., Gram negative rod). _____
- a. For cell culture deposits please complete. Is the cell being cultured in the presence of antibiotics (if so list the antibiotics) _____
- b. For hybridoma deposits please complete. What is the isotype of antibody produced? _____
- *9. Is this strain zoopathogenic? No phytopathogenic? No
10. Does this strain contain plasmids relevant to the patent process? Yes
If so, what physical containment level is required for experiments as described in the National Institutes of Health Guidelines involving Recombinant DNA Molecules (i.e., P1, P2, P3 and P4 facility)? P1
- *The answers to these questions are recommended but not required.

- FOR ATCC USE ONLY -	
ATCC DESIGNATION	_____
DATE CULTURE RECEIVED	_____
DATE VIABILITY TEST COMPLETED	_____

TO DEPOSIT OR TO CONVERT A DEPOSIT TO MEET THE REQUIREMENTS OF
BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE
DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

- *1. Name of deposit (microorganism, cell, seed, plasmid, etc.) Escherichia coli M5219
(G-pPLA-HFIF-67-12ΔMI)
2. Strain designation given by the depositor (number, symbols, etc.) HFIF-H
3. Is this an original deposit under the Budapest Treaty? _____
4. Is this a request for a conversion of a deposit already at the ATCC to meet the requirements of the Budapest Treaty? (If so, indicate ATCC designation.) Yes, ATCC 31824
5. Is this deposit a mixture of microorganisms or cells? No
6. Details and conditions necessary for the cultivation of the strain, for its storage and for testing its viability and also, where a mixture of microorganisms is deposited, descriptions of the components of the mixture and at least one of the methods permitting the checking of their presence.
see attached sheets
7. An indication of the properties of the strain which are or may be dangerous to health or the environment, or an indication that the depositor is not aware of such properties. Depositor is not aware of any properties of the strain which are or may be dangerous to health or environment.
- *8. It is recommended that sufficient description be provided to allow the ATCC to confirm that the strain deposited generally conforms to that which the depositor states is being deposited (i.e., Gram negative rod). _____
- a. For cell culture deposits please complete. Is the cell being cultured in the presence of antibiotics (if so list the antibiotics) _____
- b. For hybridoma deposits please complete. What is the isotype of antibody produced? _____
- *9. Is this strain zoopathogenic? No phytopathogenic? No
10. Does this strain contain plasmids relevant to the patent process? Yes
If so, what physical containment level is required for experiments as described in the National Institutes of Health Guidelines involving Recombinant DNA Molecules (i.e., P1, P2, P3 and P4 facility)? P1
- *The answers to these questions are recommended but not required.

— FOR ATCC USE ONLY —	
ATCC DESIGNATION	_____
DATE CULTURE RECEIVED	_____
DATE VIABILITY TEST COMPLETED	_____

AMERICAN TYPE CULTURE COLLECTION

12301 PARKLAWN DRIVE
ROCKVILLE, MARYLAND 20852

February 27, 1981

James F. Haley, Jr., Esq.
Attorney for Biogen N.V.
c/o Fish & Neave
277 Park Avenue
New York, New York 10172

Gentlemen:

We received on February 26, 1981 a deposit of cultures of organisms identified as Escherichia coli M5219(G-pPLa-HFIF-67-124MI), HFIF-H, and Escherichia coli HB101(p[325]-qHFIF-4), HFIF-I.

These strains have been assigned the ATCC numbers 31824 and 31825, respectively.

We understand that these organisms are being deposited in the American Type Culture Collection (ATCC) in connection with the filing of an application for a patent.

We further understand that the deposit of these cultures does not grant to ATCC during the effective term of the patent anticipated a license, either expressed or implied to infringe the patent, and our release of these cultures to others does not grant them a license, either expressed or implied, to infringe the patent.

We further understand that if these cultures should die or be destroyed during the effective life of the patent it shall be your responsibility to replace them with living cultures of the same organisms.

We agree in consideration for a one-time service charge, not to distribute these cultures or any information relating thereto or to their deposits until such time as a patent has been issued disclosing the above deposits except in accordance with a U.S. Patent Office Rule of Practice, Rule 14, or until you authorize us to make these strains available. After a patent is issued and we are so informed the cultures will be made available for distribution to the public. The ATCC agrees to maintain the cultures for a period of 30 years from the deposit date. Non-payment of the service charge within 90 days of the deposit date relieves the ATCC from the above provisions.

Payment in the amount of \$1,140.00 received. Thank you.

Sincerely yours,

Bobbie A. Brandon

By: (Mrs.) Bobbie A. Brandon

An independent non-profit organization incorporated in Washington, D. C. and devoted to the preservation of reference cultures and their distribution to the scientific community

1. Scientific name of organism E. coli M5219(G-pLa-HFIF-67-12AMT)
2. Strain designations other than ATCC number HFIF-H
3. Is this the type strain of this organism (see reverse side)? NO
4. If this strain has been designated in the literature as the type strain, please cite reference:

Do not write in this box	
ATCC #	<u>31821</u>
Accession date	<u>2/26/81</u>
Date received	<u>2/26/81</u>

5. Name and address of depositor: Biogen N.V.
15 Pietermaai
Curacao, Netherlands Antilles

6. Isolated by _____
from _____ date _____

7. If you did not isolate this strain, indicate from whom you received it:

ATCC ← depositor ←

8. Reason for deposit:

Requested by ATCC _____

New taxon: Species _____ Subspecies _____

Produces the antibiotic _____

Assay of _____

Production of _____

Other Patent

9. Maintenance:

Medium (attach formula) LB Broth or bactotryptone

Temperature 28°C

Other LB Broth supplemented with 50 µg/ml Kanamycin

10. a) Does this organism survive: Freeze drying? Yes Freezing? Yes (poorly)

b) Recommended method for long-term preservation:

Freeze drying or LB Broth/glycerol or DMSO at -80°C

11. Is this strain zoopathogenic? NO If so, would you classify it as class 2, 3, or 4? _____
(see reverse side for description of classes)

12. Is this strain phytopathogenic? NO (Information required by Plant Quarantine Division, USDA)

If so, a) Is the geographical distribution of this organism general, limited, or unknown (encircle)?

b) Would you recommend that this strain be made available to any qualified investigator regardless of his location? _____

c) If not, what limits would you place on the distribution of this strain?

13. Please attach a complete description of this strain unless description is given in accompanying reprint.

14. References (Please enclose two (2) of each pertinent reprint, if available):

15. Comments:

Do not heat above 28°C.

ATCC Form 1-B (1971)

J. J. H. H.
Signature of Depositor
Attorney for Biogen N.V.

1. Scientific name of organism E. coli HB101 (p[325]-αHFIF-4)
2. Strain designations other than ATCC number HFIF-I
3. Is this the type strain of this organism (see reverse side)? No
4. If this strain has been designated in the literature as the type strain, please cite reference:

Do not write in this box	
ATCC #	<u>31825</u>
Accession date	<u>2/26/81</u>
Date received	<u>2/24/81</u>

5. Name and address of depositor: Biogen N.V.
15 Pietermaai
Curacao, Netherlands Antilles

6. Isolated by _____
 from _____ date _____

7. If you did not isolate this strain, indicate from whom you received it: "

ATCC ← depositor ←

8. Reason for deposit:
 Requested by ATCC _____
 New taxon: Species _____ Subspecies _____

Produces the antibiotic _____ Assay of _____
 Production of _____ Other Patent

9. Maintenance:
 Medium (attach formula) LB Broth or bactotryptone

Temperature _____ other LB Broth supplemented with 100 μg/ml carbeniclin and/or 10 μg/ml tetracycline.

0. a) Does this organism survive: Freeze drying? Yes Freezing? Yes (poorly)
 b) Recommended method for long-term preservation:
Freeze drying or LB Broth/glycerol or DMSO at -80°C

1. Is this strain zoopathogenic? No If so, would you classify it as class 2, 3, or 4? _____
 (see reverse side for description of classes)
2. Is this strain phytopathogenic? No (Information required by Plant Quarantine Division, USDA)
 If so, a) Is the geographical distribution of this organism general, limited, or unknown (encircle)?
 b) Would you recommend that this strain be made available to any qualified investigator regardless of his location? _____
 c) If not, what limits would you place on the distribution of this strain?

3. Please attach a complete description of this strain unless description is given in accompanying reprint.

4. References (Please enclose two (2) of each pertinent reprint, if available):

5. Comments:

J. D. Haley
 Signature of Depositor
 Attorney for Biogen N.V.

ROBERT C. MORGAN
KENNETH B. HERMAN
EDWARD F. MULLOWNEY
ROBERT R. JACKSON
JESSE J. JENNER
W. EDWARD BAILEY
DAVID J. LEE
PATRICIA A. MARTONE
KEVIN J. CULLIGAN
GLENN A. OUSTERHOUT
SUSAN PROGOFF
MARGARET A. PIERRE
RON E. SHULMAN
DOUGLAS J. GILBERT
DENISE L. LORING
JEFFREY H. INGERMAN

TELECOPIER: (212) 715-0674

October 16, 1991

FREDERICK P. FISH
1855-1930
CHARLES NEAVE
1867-1937

Deutsche Sammlung von Mikroorganismen
Und Zellkulturen GmbH
Mascheroder Weg 1b
D-3300 Braunschweig
Federal Republic of Germany

Biogen - B8/B8 CIP
Deposits DSM 1791-1793; 1851-1854

Dear Sir:

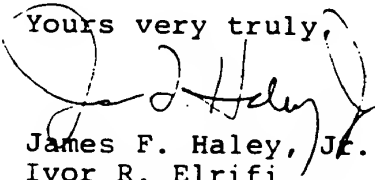
We have enclosed seven (7) applications to convert the above-identified deposits already deposited at the DSM into deposits under the Budapest Treaty. The DSM designations, as well as the strain designations given by the depositor, are identified on the application forms. In addition, we enclose copies of the "Acknowledgement of Receipt and Acceptance" forms for these deposits and the "Accession Form for Deposit" for DSM 1851-1854, containing the media and culture requirements. Please send your debit note for these conversions to my attention.

Please note that the original depositor has undergone a corporate name and address change from Biogen N.V., 24 Handelskad, Willemsted, Curacao, Netherland Antilles, to Biogen, Inc., 14 Cambridge Center, Cambridge, Massachusetts, U.S.A. 02142. This name and address change has been duly registered according to the national laws in the Patent Office of each country where a patent application has been filed referencing these deposits.

If you have any questions or require further information, please do not hesitate to contact us.

Thanks for your help.

Yours very truly,


James F. Haley, Jr.
Ivor R. Elrifi
Attorneys for Biogen, Inc.

JFH/IRE:bb
Enclosures

DAVID C. PLACNE
JANE A. HASSARD
DUANE-DAVID HUGH
MITCHELL P. BROOK
JOHN P. WARD
EDWARD J. DEFRANCO
MARK D. ROWLAND
PHILIPPE Y. RIESEN
MARK D. ENGELMANN
ERIC R. HUSBARD
DAVID A. LOEWENSTEIN
JOHN J. CASSINGHAM
LINDA A. WADLER
KELSCY I. MIX
MARTA E. GROSS
JOHN R. HINTZ
JOHN R. STORELLA
WILLIAM J. MCCABE
JOHN M. DESHARVIS
VICKIE S. VEENKER
LESLIE A. McDONELL
CHRISTOPHER P. GOOZIELA
NICOLA A. PISANO
DONALD S. REEDY
GABRIELLE E. HIGGINS
JENNIFER M. HALL
DONALD L. RHODAS
ELIZABETH M. ALDRIDGE
CLAYS. WILSON
BRENDA J. PANICHI
JEREMY LACK
EVAN M. GSELL
JAMES P. BERGIN
RONALD A. KRASHOW
JEFFREY M. KERSH
LIANNA C. KALMAR
BRADFORD L. FRIEDMAN
DEBRA A. BONTENPO
LORETTA A. MIRAGLIA
MOREY S. WILDES
CHRISTOPHER J. HARNEY
MARIE H. MACNICHOL
WILLIAM A. SCHONEMAN

To
DEUTSCHE SAMMLUNG VON MIKROORGANISMEN
UND ZELLKULTUREN GmbH
Mascheroder Weg 1b
D-3300 Braunschweig
Federal Republic of Germany

To be filled in by the Depository Authority

DSM-Accession number :

Date cultura received :

BACTERIA/FUNGI¹

THE UNDERSIGNED HEREBY DEPOSITS UNDER THE BUDAPEST TREATY THE MICROORGANISM IDENTIFIED HEREUNDER AND UNDERTAKES NOT TO WITHDRAW THE DEPOSIT FOR THE PERIOD SPECIFIED IN RULE 9.1²

I. IDENTIFICATION OF THE MICROORGANISM

Identification reference³ :

HFIF-F
M5219 (G-pPLa-HFIF-67-12Δ19)

Taxonomic designation⁴ :

Escherichia coli

The culture to be deposited is :

(X) a pure cultura

() a mixture of microorganisms

(Mark with a cross where applicable)

II. CONDITIONS FOR CULTIVATION

(X)⁵

Medium:

as according to original
deposit application DSM 1853

pH before sterilisation :

Sterilisation min at °C

pH after sterilisation:

Oxygen relationship :

() aerobic

() microaerophilic

() obligate anaerobic

Specific gaseous requirements :

Incubation temperature: °C

Incubation time:

Short term storage at: °C

Interval of transfer:

¹ The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

² This form may also be used if the undersigned converts into a deposit under the Budapest Treaty the deposit of a microorganism that he or his predecessor in title has already deposited, outside the Budapest Treaty, with the same depository institution either before (Rule 6.4(d)) or after the acquisition by that institution of the status of international depository authority.

³ Number, symbols etc., given to the microorganism by the depositor.

⁴ It is strongly recommended that the taxonomic designation and/or scientific description (see under VII.) of the microorganism be indicated.

⁵ Mark with a cross if additional information is given on an attached sheet.

IV. CONDITIONS FOR TESTING VIABILITY

(X)⁵

V. COMPONENTS OF MIXED CULTURES (WHEN APPLICABLE)

(X)⁵

Description of components:

Method(s) for checking presence of components:

⁵ Mark with a cross if additional information is given on an attached sheet.

THE STRAIN HAS TO BE HANDLED UNDER THE FOLLOWING LABORATORY CONTAINMENT LEVEL¹:

☐ L1

☐ L2

☐ L3

☐ L4

IS THIS STRAIN DANGEROUS TO HEALTH OR THE ENVIRONMENT ?

☐ YES

☒ NO

(if yes, please specify:)

☒⁵

☒ the undersigned is not aware of such properties

IF THE MICROORGANISM IS GENETICALLY MANIPULATED:

1. PLEASE INDICATE ALL THE RELEVANT GENETIC PROPERTIES:

general genetic recombination (rec):

sensitivities:

resistances:

modifications:

restrictions:

auxotrophies:

2. DESIGNATION OF THE DONOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE PLASMID:

3. If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKBS guidelines⁶ or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION).

1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINITELY HAVE NO PATHOGENIC POTENTIAL.

☐ YES

2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL.

☐ YES

IN THE LATTER CASE PLEASE NOTE:

According to the regulations of the ZKBS⁶ the DSM can only accept genetically manipulated, potentially pathogenic organisms for deposition when a copy of the permit issued by the ZKBS⁶ (or by an equivalent national biological safety commission) for work on the organisms accompanies the deposition form

¹ The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

⁵ Mark with a cross if additional information is given on an attached sheet.

⁶ ZKBS = Zentrale Kommission für Biologische Sicherheit (Central Commission for Biological safety)

VIII. ADDITIONAL DATA

()⁸IX. DEPOSITOR⁹

Name: Biogen, Inc.

Signature:

James F. Haley, Jr.
Ivor R. Elrifi
James F. Haley, Jr.
Ivor R. Elrifi
Attorneys for Biogen, Inc.
Fish & Neave
875 Third Avenue
New York, New York 10022

Address: 14 Cambridge Center
Cambridge, Massachusetts
02142

Date:

10/18/71

- ⁵ Mark with a cross if additional information is given on an attached sheet.
⁷ It is strongly recommended that the scientific description and/or proposed taxonomic designation (see 1.) of the microorganism be indicated.
⁸ Mark with a cross if additional information (other than the information referred to in footnote 4 is given on an attached sheet, such as the source of the microorganism, the name(s) and the address(es) of any other depository institution(s) with which the microorganism has been deposited, or the criterion used when drafting the proposed taxonomic designation (The supplying of such information is optional).
⁹ The name of the depositor must be identical with the signature.
In case of a legal entity the signatures of two representatives, officially nominated by this entity, are required.
Where the signature is required on behalf of a legal entity, the typewritten name(s) of the natural person(s) signing on behalf of the legal entity should accompany the signature(s).

To
DEUTSCHE SAMMLUNG VON MIKROORGANISMEN
UND ZELLKULTUREN GmbH
Mascheroder Weg 1b
D-3300 Braunschweig
Federal Republic of Germany

To be filled in by the Depository Authority

DSM-Accession number :

Date culture received :

BACTERIA/FUNGI¹

THE UNDERSIGNED HEREBY DEPOSITS UNDER THE BUDAPEST TREATY THE MICROORGANISM IDENTIFIED HEREUNDER AND UNDERTAKES NOT TO WITHDRAW THE DEPOSIT FOR THE PERIOD SPECIFIED IN RULE 9.1²

I. IDENTIFICATION OF THE MICROORGANISM		
Identification reference ³ :	The culture to be deposited is :	
HFIF-A	<input checked="" type="checkbox"/> (X) a pure culture	
HB101(G-pBR322(Pst)/HFIF 3)	<input type="checkbox"/> () a mixture of microorganisms	
Taxonomic designation ⁴ :	(Mark with a cross where applicable)	
Escherichia coli		
II. CONDITIONS FOR CULTIVATION		
<input checked="" type="checkbox"/> (X) ⁵		
Medium:	pH before sterilisation :	
as according to original	Sterilisation min at °C	
deposit application for DSM 1791	pH after sterilisation:	
	Oxygen relationship :	
	<input type="checkbox"/> () aerobic	
	<input type="checkbox"/> () microaerophilic	
	<input type="checkbox"/> () obligate anaerobic	
	Specific gaseous requirements :	
	Incubation temperature: °C	
	Incubation time:	
	Short term storage at: °C	
	Interval of transfer:	

¹ The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

² This form may also be used if the undersigned converts into a deposit under the Budapest Treaty the deposit of a microorganism that he or his predecessor in title has already deposited, outside the Budapest Treaty, with the same depository institution either before (Rule 6.4(d)) or after the acquisition by that institution of the status of international depository authority.

³ Number, symbols etc., given to the microorganism by the depositor.

⁴ It is strongly recommended that the taxonomic designation and/or scientific description (see under VII.) of the microorganism be indicated.

⁵ Mark with a cross if additional information is given on an attached sheet.

IV. CONDITIONS FOR TESTING VIABILITY

(X)⁵

V. COMPONENTS OF MIXED CULTURES (WHEN APPLICABLE)

(X)⁵

Description of components:

Method(s) for checking presence of components:

⁵ Mark with a cross if additional information is given on an attached sheet.

THE STRAIN HAS TO BE HANDLED UNDER THE FOLLOWING LABORATORY CONTAINMENT LEVEL¹:

() L1

() L2

() L3

() L4

IS THIS STRAIN DANGEROUS TO HEALTH OR THE ENVIRONMENT ?

() YES

(X) NO

(if yes, please specify:)

(X)⁵

(X) the undersigned is not aware of such properties

IF THE MICROORGANISM IS GENETICALLY MANIPULATED:

1. PLEASE INDICATE ALL THE RELEVANT GENETIC PROPERTIES:

general genetic recombination (rec):

sensitivities:

resistances:

modifications:

restrictions:

auxotrophies:

2. DESIGNATION OF THE DONOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE PLASMID:

3. If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKBS guidelines⁶ or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION).

1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINETLY HAVE NO PATHOGENIC POTENTIAL.

() YES

2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL.

() YES

IN THE LATTER CASE PLEASE NOTE:

According to the regulations of the ZKBS⁶ the DSM can only accept genetically manipulated, potentially pathogenic organisms for deposition when a copy of the permit issued by the ZKBS⁶ (or by an equivalent national biological safety commission) for work on the organisms accompanies the deposition form

¹ The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

⁵ Mark with a cross if additional information is given on an attached sheet.

⁶ ZKBS = Zentrale Kommission für Biologische Sicherheit (Central Commission for Biological safety)

VIII. ADDITIONAL DATA

()⁸IX. DEPOSITOR⁹

Name: Biogen, Inc.

Signature:

James F. Haley, Jr.
Ivor R. Elrifi
James F. Haley, Jr.
Ivor R. Elrifi
Attorneys for Biogen, Inc.
Fish & Neave
875 Third Avenue
New York, New York 10022

Address: 14 Cambridge Center
Cambridge, Massachusetts 02142

Date:

10/10/91

⁵ Mark with a cross if additional information is given on an attached sheet.⁷ It is strongly recommended that the scientific description and/or proposed taxonomic designation (see 1.) of the microorganism be indicated.⁸ Mark with a cross if additional information (other than the information referred to in footnote 4 is given on an attached sheet, such as the source of the microorganism, the name(s) and the address(es) of any other depositary institution(s) with which the microorganism has been deposited, or the criterion used when drafting the proposed taxonomic designation (The supplying of such information is optional).⁹ The name of the depositor must be identical with the signature.

In case of a legal entity the signatures of two representatives, officially nominated by this entity, are required.

Where the signature is required on behalf of a legal entity, the typewritten name(s) of the natural person(s) signing on behalf of the legal entity should accompany the signature(s).

To
DEUTSCHE SAMMLUNG VON MIKROORGANISMEN
UND ZELLKULTUREN GmbH
Mascheroder Weg 1b
D-3300 Braunschweig
Federal Republic of Germany

To be filled in by the Depository Authority

DSM-Accession number :

Date culture received :

BACTERIA/FUNGI¹

THE UNDERSIGNED HEREBY DEPOSITS UNDER THE BUDAPEST TREATY THE MICROORGANISM IDENTIFIED HEREUNDER AND UNDERTAKES NOT TO WITHDRAW THE DEPOSIT FOR THE PERIOD SPECIFIED IN RULE 9.1²

I. IDENTIFICATION OF THE MICROORGANISM		
Identification reference ³ :	The culture to be deposited is :	
HFIF-B	<input checked="" type="checkbox"/> (X) a pure culture	
HB101(G-pBR322(Pst)/HFIF 6)	<input type="checkbox"/> () a mixture of microorganisms	
Taxonomic designation ⁴ :	(Mark with a cross where applicable)	
Escherichia coli		
II. CONDITIONS FOR CULTIVATION (X)⁵		
Medium:	pH before sterilisation :	
as according to original deposit application for DSM 1792	Sterilisation	min at °C
	pH after sterilisation:	
	Oxygen relationship :	
	<input type="checkbox"/> () aerobic	
	<input type="checkbox"/> () microaerophilic	
	<input type="checkbox"/> () obligate anaerobic	
	Specific gaseous requirements :	
	Incubation temperature:	°C
	Incubation time:	
	Short term storage at:	°C
	Interval of transfer:	

¹ The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

² This form may also be used if the undersigned converts into a deposit under the Budapest Treaty the deposit of a microorganism that he or his predecessor in title has already deposited, outside the Budapest Treaty, with the same depository institution either before (Rule 6.4(d)) or after the acquisition by that institution of the status of international depository authority.

³ Number, symbols etc., given to the microorganism by the depositor.

⁴ It is strongly recommended that the taxonomic designation and/or scientific description (see under VII.) of the microorganism be indicated.

⁵ Mark with a cross if additional information is given on an attached sheet.

IV. CONDITIONS FOR TESTING VIABILITY

(X)⁵

V. COMPONENTS OF MIXED CULTURES (WHEN APPLICABLE)

(X)⁵

Description of components:

Method(s) for checking presence of components:

⁵ Mark with a cross if additional information is given on an attached sheet.

THE STRAIN HAS TO BE HANDLED UNDER THE FOLLOWING LABORATORY CONTAINMENT LEVEL¹:

☐ L1

☐ L2

☐ L3

☐ L4

IS THIS STRAIN DANGEROUS TO HEALTH OR THE ENVIRONMENT ?

☐ YES

☒ NO

(if yes, please specify:)

☒ ⁵

☒ the undersigned is not aware of such properties

IF THE MICROORGANISM IS GENETICALLY MANIPULATED:

1. PLEASE INDICATE ALL THE RELEVANT GENETIC PROPERTIES:

general genetic recombination (rec):

sensitivities:

resistances:

modifications:

restrictions:

auxotrophies:

2. DESIGNATION OF THE DONOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE PLASMID:

3. If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKBS guidelines³ or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION).

1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINITELY HAVE NO PATHOGENIC POTENTIAL.

☐ YES

2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL.

☐ YES

IN THE LATTER CASE PLEASE NOTE:

According to the regulations of the ZKBS⁶ the DSM can only accept genetically manipulated, potentially pathogenic organisms for deposition when a copy of the permit issued by the ZKBS⁶ (or by an equivalent national biological safety commission) for work on the organisms accompanies the deposition form

¹ The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

⁵ Mark with a cross if additional information is given on an attached sheet.

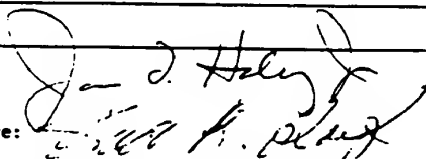
⁶ ZKBS = Zentrale Kommission für Biologische Sicherheit (Central Commission for Biological safety)

VIII. ADDITIONAL DATA

()⁸IX. DEPOSITOR⁹

Name: Biogen, Inc.

Signature:


James F. Haley, Jr.
Ivor R. Elrifi
Attorneys for Biogen, Inc.Address: 14 Cambridge Center
Cambridge, Massachusetts
02142Date: Fish & Neave
875 Third Avenue
New York, New York 10022

10/18/81

- ⁵ Mark with a cross if additional information is given on an attached sheet.
- ⁷ It is strongly recommended that the scientific description and/or proposed taxonomic designation (see 1.) of the microorganism be indicated.
- ⁸ Mark with a cross if additional information (other than the information referred to in footnote 4 is given on an attached sheet, such as the source of the microorganism, the name(s) and the address(es) of any other depository institution(s) with which the microorganism has been deposited, or the criterion used when drafting the proposed taxonomic designation (The supplying of such information is optional).
- ⁹ The name of the depositor must be identical with the signature.
In case of a legal entity the signatures of two representatives, officially nominated by this entity, are required.
Where the signature is required on behalf of a legal entity, the typewritten name(s) of the natural person(s) signing on behalf of the legal entity should accompany the signature(s).

To
DEUTSCHE SAMMLUNG VON MIKROORGANISMEN
UND ZELLKULTUREN GmbH
Mascheroder Weg 1b
D-3300 Braunschweig
Federal Republic of Germany

To be filled in by the Depository Authority

DSM-Accession number :

Date culture received :

BACTERIA/FUNGI¹

THE UNDERSIGNED HEREBY DEPOSITS UNDER THE BUDAPEST TREATY THE MICROORGANISM IDENTIFIED HEREUNDER AND UNDERTAKES NOT TO WITHDRAW THE DEPOSIT FOR THE PERIOD SPECIFIED IN RULE 9.1²

I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference ³ : HFIF-C HB101(G-pBR322(Pst)/HFIF 7) Taxonomic designation ⁴ : Escherichia coli	The culture to be deposited is : (X) a pure culture () a mixture of microorganisms (Mark with a cross where applicable)
II. CONDITIONS FOR CULTIVATION	
Medium: as according to original deposit application for DSM 1793	() ⁵ pH before sterilisation : Sterilisation min at °C pH after sterilisation: Oxygen relationship : () aerobic () microaerophilic () obligate anaerobic Specific gaseous requirements : Incubation temperature: °C Incubation time: Short term storage at: °C Interval of transfer:

¹ The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

² This form may also be used if the undersigned converts into a deposit under the Budapest Treaty the deposit of a microorganism that he or his predecessor in title has already deposited, outside the Budapest Treaty, with the same depository institution either before (Rule 6.4(d)) or after the acquisition by that institution of the status of international depository authority.

³ Number, symbols etc., given to the microorganism by the depositor.

⁴ It is strongly recommended that the taxonomic designation and/or scientific description (see under VII.) of the microorganism be indicated.

⁵ Mark with a cross if additional information is given on an attached sheet.

IV. CONDITIONS FOR TESTING VIABILITY

(X)⁵

V. COMPONENTS OF MIXED CULTURES (WHEN APPLICABLE)

(X)⁵

Description of components:

Method(s) for checking presence of components:

⁵ Mark with a cross if additional information is given on an attached sheet.

THE STRAIN HAS TO BE HANDLED UNDER THE FOLLOWING LABORATORY CONTAINMENT LEVEL¹:

() L1

() L2

() L3

() L4

IS THIS STRAIN DANGEROUS TO HEALTH OR THE ENVIRONMENT ?

() YES

(X) NO

(if yes, please specify:)

(X)⁵

(X) the undersigned is not aware of such properties

IF THE MICROORGANISM IS GENETICALLY MANIPULATED:

1. PLEASE INDICATE ALL THE RELEVANT GENETIC PROPERTIES:

general genetic recombination (rec):

sensitivities:

resistances:

modifications:

restrictions:

auxotrophies:

2. DESIGNATION OF THE DONOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE PLASMID:

3. If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKBS guidelines⁶ or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION).

1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINITELY HAVE NO PATHOGENIC POTENTIAL.

() YES

2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL.

() YES

IN THE LATTER CASE PLEASE NOTE:

According to the regulations of the ZKBS⁶ the DSM can only accept genetically manipulated, potentially pathogenic organisms for deposition when a copy of the permit issued by the ZKBS⁶ (or by an equivalent national biological safety commission) for work on the organisms accompanies the deposition form

¹ The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

⁵ Mark with a cross if additional information is given on an attached sheet.

⁶ ZKBS = Zentrale Kommission für Biologische Sicherheit (Central Commission for Biological safety)

VIII. ADDITIONAL DATA

()⁸IX. DEPOSITOR⁹

Name: Biogen, Inc.

Signature: 

James F. Haley, Jr.
Ivor R. Elrifi
Attorneys for Biogen, Inc.
Fish & Neave
875 Third Avenue
New York, New York 10022

Address: 14 Cambridge Center
Cambridge, Massachusetts
02142

Date:

12/18/91

- ⁵ Mark with a cross if additional information is given on an attached sheet.
⁷ It is strongly recommended that the scientific description and/or proposed taxonomic designation (see 1.) of the microorganism be indicated.
⁸ Mark with a cross if additional information (other than the information referred to in footnote 4 is given on an attached sheet, such as the source of the microorganism, the name(s) and the address(es) of any other depository institution(s) with which the microorganism has been deposited, or the criterion used when drafting the proposed taxonomic designation (The supplying of such information is optional).
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To
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UND ZELLKULTUREN GmbH
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Federal Republic of Germany

To be filled in by the Depositary Authority

DSM-Accession number :

Date culture received :

BACTERIA/FUNGI¹

THE UNDERSIGNED HEREBY DEPOSITS UNDER THE BUDAPEST TREATY THE MICROORGANISM IDENTIFIED HEREUNDER AND UNDERTAKES NOT TO WITHDRAW THE DEPOSIT FOR THE PERIOD SPECIFIED IN RULE 9.1²

I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference ³ : HFIF-G M5219 (G-pPLc-HFIF-67-8) Taxonomic designation ⁴ : Escherichia coli	The culture to be deposited is : (X) a pure culture () a mixture of microorganisms (Mark with a cross where applicable)
II. CONDITIONS FOR CULTIVATION	
Medium: as according to original deposit application DSM 1854	(X) ⁵ pH before sterilisation : Sterilisation min at °C pH after sterilisation: Oxygen relationship : () aerobic () microaerophilic () obligate anaerobic Specific gaseous requirements : Incubation temperature: °C Incubation time: Short term storage at: °C Interval of transfer:

¹ The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

² This form may also be used if the undersigned converts into a deposit under the Budapest Treaty the deposit of a microorganism that he or his predecessor in title has already deposited, outside the Budapest Treaty, with the same depositary institution either before (Rule 6.4(d)) or after the acquisition by that institution of the status of international depositary authority.

³ Number, symbols etc., given to the microorganism by the depositor.

⁴ It is strongly recommended that the taxonomic designation and/or scientific description (see under VII.) of the microorganism be indicated.

⁵ Mark with a cross if additional information is given on an attached sheet.

IV. CONDITIONS FOR TESTING VIABILITY

(X)⁵

V. COMPONENTS OF MIXED CULTURES (WHEN APPLICABLE)

(X)⁵

Description of components:

Method(s) for checking presence of components:

⁵ Mark with a cross if additional information is given on an attached sheet.

THE STRAIN HAS TO BE HANDLED UNDER THE FOLLOWING LABORATORY CONTAINMENT LEVEL¹:

() L1

() L2

() L3

() L4

IS THIS STRAIN DANGEROUS TO HEALTH OR THE ENVIRONMENT ?

() YES

(X) NO

(if yes, please specify:)

(X)⁵

(X) the undersigned is not aware of such properties

IF THE MICROORGANISM IS GENETICALLY MANIPULATED:

1. PLEASE INDICATE ALL THE RELEVANT GENETIC PROPERTIES:

general genetic recombination (rec):

sensitivities:

resistances:

modifications:

restrictions:

auxotrophies:

2. DESIGNATION OF THE DONOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE PLASMID:

3. If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKBS guidelines⁶ or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION).

1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINETLY HAVE NO PATHOGENIC POTENTIAL.

() YES

2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL.

() YES

IN THE LATTER CASE PLEASE NOTE:

According to the regulations of the ZKBS⁶ the DSM can only accept genetically manipulated, potentially pathogenic organisms for deposition when a copy of the permit issued by the ZKBS⁶ (or by an equivalent national biological safety commission) for work on the organisms accompanies the deposition form

¹ The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vpr Gefahren durch in-vitro neukombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

⁵ Mark with a cross if additional information is given on an attached sheet.

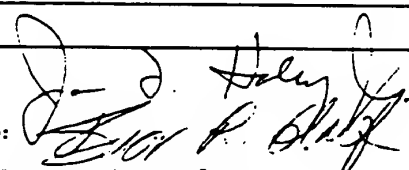
⁶ ZKBS = Zentrale Kommission für Biologische Sicherheit (Central Commission for Biological safety)

VIII. ADDITIONAL DATA

()⁸IX. DEPOSITOR⁹

Name: Biogen, Inc.

Signature:


James F. Haley, Jr.
Ivor R. Elrifi
Attorneys for Biogen, Inc.Address: 14 Cambridge Center
Cambridge, Massachusetts
02142

Date:

Fish & Neave
875 Third Avenue
New York, New York 10022

10/1/82

- ⁵ Mark with a cross if additional information is given on an attached sheet.
⁷ It is strongly recommended that the scientific description and/or proposed taxonomic designation (see 1.) of the microorganism be indicated.
⁸ Mark with a cross if additional information (other than the information referred to in footnote 4 is given on an attached sheet, such as the source of the microorganism, the name(s) and the address(es) of any other depository institution(s) with which the microorganism has been deposited, or the criterion used when drafting the proposed taxonomic designation (The supplying of such information is optional).
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To
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UND ZELLKULTUREN GmbH
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D-3300 Braunschweig
Federal Republic of Germany

To be filled in by the Depositary Authority

DSM-Accession number :

Date culture received :

BACTERIA/FUNGI¹

THE UNDERSIGNED HEREBY DEPOSITS UNDER THE BUDAPEST TREATY THE MICROORGANISM IDENTIFIED HEREUNDER AND UNDERTAKES NOT TO WITHDRAW THE DEPOSIT FOR THE PERIOD SPECIFIED IN RULE 9.1²

I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference ³ : HFIF-D M5219 (G-pPLa-HFIF-67-12) Taxonomic designation ⁴ : Escherichia coli	The culture to be deposited is : (X) a pure culture () a mixture of microorganisms (Mark with a cross where applicable)
II. CONDITIONS FOR CULTIVATION (X) ⁵	
Medium: as according to original deposit application for DSM 1851	pH before sterilisation : Sterilisation min at °C pH after sterilisation: Oxygen relationship : () aerobic () microaerophilic () obligate anaerobic Specific gaseous requirements : Incubation temperature: °C Incubation time: Short term storage at: °C Interval of transfer:

¹ The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

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³ Number, symbols etc., given to the microorganism by the depositor.

⁴ It is strongly recommended that the taxonomic designation and/or scientific description (see under VII.) of the microorganism be indicated.

⁵ Mark with a cross if additional information is given on an attached sheet.

IV. CONDITIONS FOR TESTING VIABILITY

(X)⁵

V. COMPONENTS OF MIXED CULTURES (WHEN APPLICABLE)

(X)⁵

Description of components:

Method(s) for checking presence of components:

⁵ Mark with a cross if additional information is given on an attached sheet.

THE STRAIN HAS TO BE HANDLED UNDER THE FOLLOWING LABORATORY CONTAINMENT LEVEL¹:

() L1

() L2

() L3

() L4

IS THIS STRAIN DANGEROUS TO HEALTH OR THE ENVIRONMENT ?

() YES

(X) NO

(if yes, please specify:)

(X)⁵

(X) the undersigned is not aware of such properties

IF THE MICROORGANISM IS GENETICALLY MANIPULATED:

1. PLEASE INDICATE ALL THE RELEVANT GENETIC PROPERTIES:

general genetic recombination (rec):

sensitivities:

resistances:

modifications:

restrictions:

auxotrophies:

2. DESIGNATION OF THE DONOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE PLASMID:

3. If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKBS guidelines⁶ or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION).

1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINITELY HAVE NO PATHOGENIC POTENTIAL.

() YES

2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL.

() YES

IN THE LATTER CASE PLEASE NOTE:

According to the regulations of the ZKBS⁶ the DSM can only accept genetically manipulated, potentially pathogenic organisms for deposition when a copy of the permit issued by the ZKBS⁶ (or by an equivalent national biological safety commission) for work on the organisms accompanies the deposition form

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⁵ Mark with a cross if additional information is given on an attached sheet.

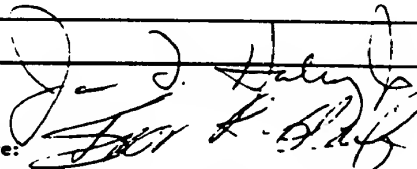
⁶ ZKBS = Zentrale Kommission für Biologische Sicherheit (Central Commission for Biological safety)

VIII. ADDITIONAL DATA

()⁸IX. DEPOSITOR⁹

Name: Biogen, Inc.

Signature:


James F. Haley, Jr.
Ivor R. Elrifi
Attorneys for Biogen, Inc.Address: 14 Cambridge Center
Cambridge, Massachusetts
02142Date: Fish & Neave
875 Third Avenue
New York, New York 10022

12/13/91

⁵ Mark with a cross if additional information is given on an attached sheet.⁷ It is strongly recommended that the scientific description and/or proposed taxonomic designation (see I.) of the microorganism be indicated.⁸ Mark with a cross if additional information (other than the information referred to in footnote 4 is given on an attached sheet, such as the source of the microorganism, the name(s) and the address(es) of any other depositary institution(s) with which the microorganism has been deposited, or the criterion used when drafting the proposed taxonomic designation (The supplying of such information is optional).⁹ The name of the depositor must be identical with the signature.

In case of a legal entity the signatures of two representatives, officially nominated by this entity, are required.

Where the signature is required on behalf of a legal entity, the typewritten name(s) of the natural person(s) signing on behalf of the legal entity should accompany the signature(s).

To
DEUTSCHE SAMMLUNG VON MIKROORGANISMEN
UND ZELLKULTUREN GmbH
Mascheroder Weg 1b
D-3300 Braunschweig
Federal Republic of Germany

To be filled in by the Depository Authority

DSM-Accession number :

Date culture received :

BACTERIA/FUNGI¹

THE UNDERSIGNED HEREBY DEPOSITS UNDER THE BUDAPEST TREATY THE MICROORGANISM IDENTIFIED HEREUNDER AND UNDERTAKES NOT TO WITHDRAW THE DEPOSIT FOR THE PERIOD SPECIFIED IN RULE 9.1²

I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference ³ : HFIF-E K12ΔHI (G-pPLa-HFIF-67-12) Taxonomic designation ⁴ : Escherichia coli	The culture to be deposited is : (X) a pure culture () a mixture of microorganisms (Mark with a cross where applicable)
II. CONDITIONS FOR CULTIVATION	
(X) ⁵	
Medium: as according to original deposit application for DSM 1852	pH before sterilisation : Sterilisation min at °C pH after sterilisation: Oxygen relationship : () aerobic () microaerophilic () obligate anaerobic Specific gaseous requirements : Incubation temperature: °C Incubation time: Short term storage at: °C Interval of transfer:

¹ The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

² This form may also be used if the undersigned converts into a deposit under the Budapest Treaty the deposit of a microorganism that he or his predecessor in title has already deposited, outside the Budapest Treaty, with the same depository institution either before (Rule 6.4(d)) or after the acquisition by that institution of the status of international depository authority.

³ Number, symbols etc., given to the microorganism by the depositor.

⁴ It is strongly recommended that the taxonomic designation and/or scientific description (see under VII.) of the microorganism be indicated.

⁵ Mark with a cross if additional information is given on an attached sheet.

IV. CONDITIONS FOR TESTING VIABILITY

(X)⁵

V. COMPONENTS OF MIXED CULTURES (WHEN APPLICABLE)

(X)⁵

Description of components:

Method(s) for checking presence of components:

⁵ Mark with a cross if additional information is given on an attached sheet.

THE STRAIN HAS TO BE HANDLED UNDER THE FOLLOWING LABORATORY CONTAINMENT LEVEL¹:

☐ L1

☐ L2

☐ L3

☐ L4

IS THIS STRAIN DANGEROUS TO HEALTH OR THE ENVIRONMENT ?

☐ YES

☒ NO

(if yes, please specify:)

☒⁵

☒ the undersigned is not aware of such properties

IF THE MICROORGANISM IS GENETICALLY MANIPULATED:

1. PLEASE INDICATE ALL THE RELEVANT GENETIC PROPERTIES:

general genetic recombination (rec):

sensitivities:

resistances:

modifications:

restrictions:

auxotrophies:

2. DESIGNATION OF THE DONOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE PLASMID:

3. If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKBS guidelines⁶ or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION).

1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINITELY HAVE NO PATHOGENIC POTENTIAL.

☐ YES

2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL.

☐ YES

IN THE LATTER CASE PLEASE NOTE:

According to the regulations of the ZKBS⁶ the DSM can only accept genetically manipulated, potentially pathogenic organisms for deposition when a copy of the permit issued by the ZKBS⁶ (or by an equivalent national biological safety commission) for work on the organisms accompanies the deposition form

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⁵ Mark with a cross if additional information is given on an attached sheet.

⁶ ZKBS = Zentrale Kommission für Biologische Sicherheit (Central Commission for Biological safety)

VIII. ADDITIONAL DATA

(,⁸IX. DEPOSITOR⁹

Name: Biogen, Inc.

Signature:

James F. Haley, Jr.
Ivor R. Elrifi
James F. Haley, Jr.
Ivor R. Elrifi
Attorneys for Biogen, Inc.
Fish & Neave
875 Third Avenue
New York, New York 10022

Address: 14 Cambridge Center
Cambridge, Massachusetts
02142

Date:

10/12/71

- ⁵ Mark with a cross if additional information is given on an attached sheet.
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⁸ Mark with a cross if additional information (other than the information referred to in footnote 4 is given on an attached sheet, such as the source of the microorganism, the name(s) and the address(es) of any other depository institution(s) with which the microorganism has been deposited, or the criterion used when drafting the proposed taxonomic designation (The supplying of such information is optional).
⁹ The name of the depositor must be identical with the signature.
In case of a legal entity the signatures of two representatives, officially nominated by this entity, are required.
Where the signature is required on behalf of a legal entity, the typewritten name(s) of the natural person(s) signing on behalf of the legal entity should accompany the signature(s).

The deposit is made in accordance with Rule 28 EPC / with the Swedish patent legislation (delete, if not applicable)

Name and address of depositor:

BIOGEN N.V.
24 Handelskad
Willemsted
Curacao, Netherland Antilles

Identification reference of the microorganism given by the depositor (strain number, symbols etc.):

HFIF-D
M 5219 (G-p PL2 - HFIF-67-12)

Taxonomic designation of the microorganism:

E. coli

A scientific description of the microorganism is attached on a separate sheet:

YES ☐

NO ☒

The microorganism to be deposited is

a pure culture

YES ☒

NO ☐

a mixture of strains :

YES ☐

NO ☒

In case of a mixed culture, please give a concise description on a separate sheet about the components and methods to determine their viability.

Does the microorganism and/or its metabolic products present any hazard for man, animals, plants or the environment: (if any, please specify on a separate sheet):

YES ☐

NO ☒

☒ The microorganism will be ~~sent~~ ^{hand delivered} to the DSM directly by the depositor.

☐ The microorganism will be sent to the DSM on behalf of the depositor by the following depository under the designation and accession number given:

The microorganism may be rendered accessible after receipt and deposition to any third party

☐ without any restriction

☒ according to Rule 28 EPC and to the agreement between the European Patent Organisation and the DSM (Official Journal EPO 5, 301-307, 1978) and/or

☒ according to the Swedish patent legislation and to the agreement between the Swedish Patent Office and the DSM (Svensk Patenttidning nr 12, 1979)

☒ in accordance with the "Declaration of Release" to be filed by the depositor with the DSM and the German Patent Office (at present Form 2750)

☒ in accordance with a) Title 37, Code of Federal Regulations, Section 1.14 (37.CFR 1.14) and Title 35, United States Code section 122 (35 U.S.C. 122) of the United States of America and b) without any restrictions on the availability to the public of the culture upon granting of the United States patent wherein the deposited microorganism is part of the disclosure of the invention.

☒ in accordance with the French patent law

☐ in accordance with the conditions as specified by the depositor on enclosed separate sheet.

(Please mark what applies)

P.T.O.

Temperature: 28°C

Incubation time:

Short-term storage at 4 °C

Interval of transfer: Never exceed

Liquid culture

stationary ☐ shaker ☐

Agar culture

plate ☐ slant ☐ stab ☒

Any other method:

Long term preservation:

Freeze drying ☐

, liquid nitrogen storage ☒

, other (please specify) ☐

Pre-drying/freezing medium:

Time and temperature of incubation:

Suspending fluid:

Recovery medium:

(Viability testing)

Additional remarks:

Gent 4 June 1980

Place

date

W E Bailey

Signature of depositor

Attorney for BIOGEN N.V.

The deposit is made in accordance with Rule 28 EPC / with the Swedish patent legislation (delete, if not applicable)

Name and address of depositor:

BIOGEN N.V.
24 Handelskad
Willemsted
Curacao, Netherland Antilles

Identification reference of the microorganism given by the depositor (strain number, symbols etc.):

HFIF - E

K12ΔHI (G-pLα - HFIF - 67-12)

Taxonomic designation of the microorganism:

E. coli

A scientific description of the microorganism is attached on a separate sheet:

YES ☐

NO ☒

The microorganism to be deposited is

a pure culture

YES ☒

NO ☐

a mixture of strains :

YES ☐

NO ☒

In case of a mixed culture, please give a concise description on a separate sheet about the components and methods to determine their viability.

Does the microorganism and/or its metabolic products present any hazard for man, animals, plants or the environment: (if any, please specify on a separate sheet):

YES ☐

NO ☒

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☒ in accordance with the French patent law

☐ in accordance with the conditions as specified by the depositor on enclosed separate sheet.

(Please mark what applies)

P.T.O.

Temperature: 28°C

Incubation time:

Short-term storage at 4 °C

Interval of transfer:

Never exceed:

Liquid culture

stationary ☐ shaker ☐

Agar culture

plate ☐ slant ☐ slant ☒

Any other method:

Long term preservation:

Freeze drying ☐

, liquid nitrogen storage ☒

, other (please specify) ☐

Pre-drying/freezing medium:

Time and temperature of incubation:

Suspending fluid:

Recovery medium:

(Viability testing)

Additional remarks:

Gent 4 June 1980

Place

date

W.B. Bailey

Signature of depositor

Attorney for BIOGEN N.V.

The deposit is made in accordance with Rule 28 EPC / with the Swedish patent legislation (delete, if not applicable)

Name and address of depositor:

BIOGEN N.V.
24 Handelskad
Willemsted
Curacao, Netherland Antilles

Identification reference of the microorganism given by the depositor (strain number, symbols etc.):

HFIF - F
M5219 (G - pPLa - HFIF - 67-12 Δ19)

Taxonomic designation of the microorganism:

A scientific description of the microorganism is attached on a separate sheet:

YES ☐

NO ☒

The microorganism to be deposited is

a pure culture

YES ☒

NO ☐

a mixture of strains :

YES ☐

NO ☒

In case of a mixed culture, please give a concise description on a separate sheet about the components and methods to determine their viability.

Does the microorganism and/or its metabolic products present any hazard for man, animals, plants or the environment: (if any, please specify on a separate sheet):

YES ☐

NO ☒

- ☒ The microorganism will be ^{hand delivered} sent to the DSM directly by the depositor.
- ☐ The microorganism will be sent to the DSM on behalf of the depositor by the following depository under the designation and accession number given:

The microorganism may be rendered accessible after receipt and deposition to any third party

☐ without any restriction

☒ according to Rule 28 EPC and to the agreement between the European Patent Organisation and the DSM (Official Journal EPJ 2, 301-307, 1978) and/or

☒ according to the Swedish patent legislation and to the agreement between the Swedish Patent Office and the DSM (Svensk Patenttidning nr 12, 1979)

☒ in accordance with the "Declaration of Release" to be filed by the depositor with the DSM and the German Patent Office (at present Form 2750)

☒ in accordance with a) Title 37, Code of Federal Regulations, Section 1.14 (37.CFR 1.14) and Title 35, United States Code section 122 (35 U.S.C. 122) of the United States of America and b) without any restrictions on the availability to the public of the culture upon granting of the United States patent wherein the deposited microorganism is part of the disclosure of the invention

☒ in accordance with the French patent law

☐ in accordance with the conditions as specified by the depositor on enclosed separate sheet.

(Please mark what applies)

P.T.O.

Temperature: 28 °C

Incubation time:

Short-term storage at 4 °C

Interval of transfer:

Never exceed 28°

Liquid culture

stationary ☐ shaker ☐

Agar culture

plate ☐ slant ☐ stab ☒

Any other method:

Long term preservation:

Freeze drying ☐ , liquid nitrogen storage ☒ , other (please specify) ☐

Pre-drying/freezing medium:

Time and temperatur of incubation:

Suspending fluid:

Recovery medium:

(Viability testing)

Additional remarks:

Gent 4 June 1980

Place

date

W E Sailer

Signature of depositor

Attorney for BIOGEN N.V.

The deposit is made in accordance with Rule 28 EPC / with the Swedish patent legislation (delete, if not applicable)

Name and address of depositor:

BIOGEN N.V.
24 Handelskad
Willemsted
Curacao, Netherland Antilles

Identification reference of the microorganism given by the depositor (strain number, symbols etc.):

HFIF - G
M5219 (G- pPLc - HFIF - 67-8)

Taxonomic designation of the microorganism:

E. coli

A scientific description of the microorganism is attached on a separate sheet:

YES ☐

NO ☒

The microorganism to be deposited is

a pure culture

YES ☒

NO ☐

a mixture of strains :

YES ☐

NO ☒

In case of a mixed culture, please give a concise description on a separate sheet about the components and methods to determine their viability.

Does the microorganism and/or its metabolic products present any hazard for man, animals, plants or the environment: (if any, please specify on a separate sheet):

YES ☐

NO ☒

☒ The microorganism will be ~~sent~~ ^{hand delivered} to the DSM directly by the depositor.

☐ The microorganism will be sent to the DSM on behalf of the depositor by the following depository under the designation and accession number given:

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☒ according to the Swedish patent legislation and to the agreement between the Swedish Patent Office and the DSM (Svensk Patenttidning nr 12, 1979)

☒ in accordance with the "Declaration of Release" to be filed by the depositor with the DSM and the German Patent Office (at present Form 2750)

☒ in accordance with a) Title 37, Code of Federal Regulations, Section 1.14 (37.CFR 1.14) and Title 35, United States Code section 122 (35 U.S.C. 122) of the United States of America and b) without any restrictions on the availability to the public of the culture upon granting of the United States patent wherein the deposited microorganism is part of the disclosure of the invention

☒ in accordance with the French patent law

☐ in accordance with the conditions as specified by the depositor on enclosed separate sheet.

(Please mark what applies)

P.T.O.

temperature: 28 °C

Incubation time:

Short-term storage at 4 °C

Interval of transfer:

Never exceed 28

Liquid culture

stationary ☐ shaker ☐

Agar culture

plate ☐ slant ☐ stab ☒

Any other method:

Long term preservation:

Freeze drying ☐

, liquid nitrogen storage ☒

, other (please specify) ☐

Pre-drying/freezing medium:

Time and temperature of incubation:

Suspending fluid:

Recovery medium:

(Viability testing)

Additional remarks:

Gent 4 June 1980

Place

date

W.B. Bailey

Signature of depositor

Attorney for BIOGEN N.V.

ACKNOWLEDGEMENT OF RECEIPT AND ACCEPTANCE

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikroorganismen.

Name and address
of depositor:

Biogen N.V.
24 Handelskad
Willemsted
Curacao, Netherland Antilles

Identification reference of
the microorganism used by
the depositor:

HFIF-8
HB101(G-pBR322(Pst)/HFIF 6)

Taxonomic designation of
the microorganism provi-
ded by the depositor:

Escherichia coli

DSM accession number of
the microorganism:

DSM 1792

Date of receipt of the
viable microorganism:

April 2, 1980 -

In addition to the identification reference and the taxonomic designation the depositor ~~XXX~~
~~XXXXXXX~~ has not provided a scientific description of the microorganism.

- ☒ The microorganism has been sent to the DSM directly by the depositor.
☐ The microorganism has been sent to the DSM on behalf of the depositor by the following
depository under the designation and accession number given:

As stated by the depositor the microorganism may be rendered accessible to any third party
under the following conditions:

- ☐ without any restrictions
☒ according to Rule 28 EPC and to the agreement between the European Patent Organisation
and the DSM (Official Journal EPO 5, 301-307, 1978) and/or
☒ according to the Swedish patent legislation and to the agreement between the Swedish
Patent Office and the DSM (Svensk Patenttidning nr 12, 1979)
☒ in accordance with the "Declaration of Release" to be filed by the depositor with the
DSM and the German Patent Office (at present Form P 2570)
☒ in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14)
and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of
America and b) without any restriction on availability to the public of the culture
upon granting of a United States patent wherein the deposited microorganism is part
of the disclosure of the invention
☒ in accordance with the French patent law
☐ in accordance with the conditions as specified by the depositor on enclosed separate
sheet.

Göttingen, April 2, 1980

Place — date DEUTSCHE SAMMLUNG VON MIKROORGANISMEN Signature
der
Gesellschaft für Biotechnologische Forschung mbH
Grisebachstraße 8
D-3400 Göttingen

Gesellschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig, Tel: (05 31) 70 08-1, Telex: 9-5 26 67

Vorsitzender des Aufsichtsrats:
Min. Dir. Dr. Friedrich Bischoff

Geschäftsführer:
Dr. Maria-Regina Kula
Dr. Helmut Zellträger

Bankkonto:
Gebr. Lohbeck, Braunschweig
Konto 23 781 (BLZ 270 305 00)

Registergericht:
Amtsgericht Braunschweig
HRB 477

ACKNOWLEDGEMENT OF RECEIPT AND ACCEPTANCE

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikroorganismen.

Name and address
of depositor:

Biogen N.V.
24 Handelskad
Willemsted
Curacao, Netherland Antilles

Identification reference of
the microorganism used by
the depositor:

HFIF-C
HB101(G-pBR322(Pst)/HFIF 7)

Taxonomic designation of
the microorganism provi-
ded by the depositor:

Escherichia coli

DSM accession number of
the microorganism:

DSM 1793

Date of receipt of the
viable microorganism:

April 2, 1980

In addition to the identification reference and the taxonomic designation the depositor ^{XXX}has provided / has not provided a scientific description of the microorganism.

- ☒ The microorganism has been sent to the DSM directly by the depositor.
☐ The microorganism has been sent to the DSM on behalf of the depositor by the following depository under the designation and accession number given:

As stated by the depositor the microorganism may be rendered accessible to any third party under the following conditions:

- ☐ without any restrictions
☒ according to Rule 28 EPC and to the agreement between the European Patent Organisation and the DSM (Official Journal EPO 5, 301-307, 1978) and/or
☒ according to the Swedish patent legislation and to the agreement between the Swedish Patent Office and the DSM (Svensk Patenttidning nr 12, 1979)
☒ in accordance with the "Declaration of Release" to be filed by the depositor with the DSM and the German Patent Office (at present Form P 2570)
☐ in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14) and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of America and b) without any restriction on availability to the public of the culture upon granting of a United States patent wherein the deposited microorganism is part of the disclosure of the invention
☒ in accordance with the French patent law
☐ in accordance with the conditions as specified by the depositor on enclosed separate sheet.

Göttingen, April 2, 1980

Place

date

DEUTSCHE SAMMLUNG VON MIKROORGANISMEN

der

Gesellschaft für Biotechnologische Forschung mbH
Grisebachstraße 8

D-3400 Göttingen

Gesellschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig, Tel: (05 31) 70 08-1, Telex: 9-5 26 67

Vorsitzender des Aufsichtsrats:
Min. Dir. Dr. Friedrich Bischoff

Geschäftsführer:
Dr. Maria-Regina Kula
Dr. Helmut Zenträger

Bankkonto:
Gebr. Löbbecke, Braunschweig
Konto 23 781 (BLZ 270 305 00)

Registergericht:
Amtsgericht Braunschweig
HRB 477

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikroorganismen.

Name and address
of depositor:

BIOGEN N.V.
24 Handelskad
Willemsted,
Curacao, Netherland Antilles

Identification reference of
the microorganism used by
the depositor:

HFIF-D
M5219 (G-pPLa-HFIF-67-12)

Taxonomic designation of
the microorganism provi-
ded by the depositor:

Escherichia coli

DSM accession number of
the microorganism:

DSM 1851

Date of receipt of the
viable microorganism:

June 5, 1980

In addition to the identification reference and the taxonomic designation the depositor ~~has~~ / has not provided a scientific description of the microorganism.

- ☒ The microorganism has been sent to the DSM directly by the depositor.
☐ The microorganism has been sent to the DSM on behalf of the depositor by the following depository under the designation and accession number given:

As stated by the depositor the microorganism may be rendered accessible to any third party under the following conditions:

- ☐ without any restrictions
☒ according to Rule 28 EPC and to the agreement between the European Patent Organisation and the DSM (Official Journal EPD 5, 301-307, 1978) and/or
☒ according to the Swedish patent legislation and to the agreement between the Swedish Patent Office and the DSM (Svensk Patenttidning nr 12, 1979)
☒ in accordance with the "Declaration of Release" to be filed by the depositor with the DSM and the German Patent Office (at present Form P 2570)
☒ in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14) and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of America and b) without any restriction on availability to the public of the culture upon granting of a United States patent wherein the deposited microorganism is part of the disclosure of the invention
☒ in accordance with the French patent law
☐ in accordance with the conditions as specified by the depositor on enclosed separate sheet.

Göttingen, June 5, 1980

Place

date

DEUTSCHE SAMMLUNG VON MIKROORGANISMEN

der

Signature

Gesellschaft für Biotechnologische Forschung mbH
Grisebachstraße 8

D-3400 Göttingen

Gesellschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig, Tel.: (05 31) 70 08-1, Telex: 9-5 28 67

Vorsitzender des Aufsichtsrats:
Min. Dr. Dr. Friedrich Bischoff

Geschäftsführer:
Dr. Maria-Regina Kula
Dr. Helmut Zentträger

Bankkonto:
Gebr. Lobbecke, Braunschweig
Konto 23 781 (BLZ 270 305 00)

Registriergericht:
Amtsgericht Braunschweig
HRB 477

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikroorganismen.

Name and address
of depositor:

BIOGEN N.V.
24 Handelskad-
Willemsted,
Curacao, Netherland Antilles
HFIF-E
K12ΔHI (G-pPLa-HFIF-67-12)

Identification reference of
the microorganism used by
the depositor:

Taxonomic designation of
the microorganism provi-
ded by the depositor:

Escherichia coli

DSM accession number of
the microorganism:

DSM 1852

Date of receipt of the
viable microorganism:

June 5, 1980

In addition to the identification reference and the taxonomic designation the depositor ~~has~~ ^{has} not provided a scientific description of the microorganism.

- ☒ The microorganism has been sent to the DSM directly by the depositor.
☐ The microorganism has been sent to the DSM on behalf of the depositor by the following depository under the designation and accession number given:

As stated by the depositor the microorganism may be rendered accessible to any third party under the following conditions:

- ☐ without any restrictions
☒ according to Rule 28 EPC and to the agreement between the European Patent Organisation and the DSM (Official Journal EPO 5, 301-307, 1978) and/or
☒ according to the Swedish patent legislation and to the agreement between the Swedish Patent Office and the DSM (Svensk Patenttidning nr 12, 1979)
☒ in accordance with the "Declaration of Release" to be filed by the depositor with the DSM and the German Patent Office (at present Form P 2570)
☒ in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14) and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of America and b) without any restriction on availability to the public of the culture upon granting of a United States patent wherein the deposited microorganism is part of the disclosure of the invention
☒ in accordance with the French patent law
☐ in accordance with the conditions as specified by the depositor on enclosed separate sheet.

Göttingen, June 5, 1980

Place

date

DEUTSCHE SAMMLUNG VON MIKROORGANISMEN

der

Signature

Gesellschaft für Biotechnologische Forschung mbH
Grisebachstraße 8
D-3400 Göttingen

Gesellschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig. Tel.: (05 31) 70 08-1. Telex: 9-5 28 87

Vorsitzender des Aufsichtsrats:
Min. Dir. Dr. Friedrich Bischoff

Geschäftsführer:
Dr. Maria-Regina Kula
Dr. Helmut Zentgraf

Bankkonto:
Gebr. Löbbecke, Braunschweig
Konto 23 781 (BLZ 270 305 00)

Registergericht:
Amtsgericht Braunschweig
HRB 477

ACKNOWLEDGEMENT OF RECEIPT AND ACCEPTANCE

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikroorganismen.

Name and address
of depositor:

BIOGEN N.V.
24 Handelskad
Willemsted,
Curacao, Netherland Antilles

Identification reference of
the microorganism used by
the depositor:

HFIF-F
M5219 (G-pPLa -HFIF-67-12419)

Taxonomic designation of
the microorganism provi-
ded by the depositor:

Escherichia coli

DSM accession number of
the microorganism:

DSM 1853

Date of receipt of the
viable microorganism:

June 5, 1980

In addition to the identification reference and the taxonomic designation the depositor ~~has~~ provided / has not provided a scientific description of the microorganism.

- ☒ The microorganism has been sent to the DSM directly by the depositor.
☐ The microorganism has been sent to the DSM on behalf of the depositor by the following depository under the designation and accession number given:

As stated by the depositor the microorganism may be rendered accessible to any third party under the following conditions:

- ☐ without any restrictions
☒ according to Rule 28 EPC and to the agreement between the European Patent Organisation and the DSM (Official Journal EPO 5, 301-307, 1978) and/or
☒ according to the Swedish patent legislation and to the agreement between the Swedish Patent Office and the DSM (Svensk Patenttidning nr 12, 1979)
☒ in accordance with the "Declaration of Release" to be filed by the depositor with the DSM and the German Patent Office (at present Form P 2570)
☒ in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14) and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of America and b) without any restriction on availability to the public of the culture upon granting of a United States patent wherein the deposited microorganism is part of the disclosure of the invention
☒ in accordance with the French patent law
☐ in accordance with the conditions as specified by the depositor on enclosed separate sheet.

Göttingen, June 5, 1980

D. Ower

Place date **DEUTSCHE SAMMLUNG VON MIKROORGANISMEN** Signature
der
Gesellschaft für Biotechnologische Forschung mbH
Grisebachstraße 8
D-3400 Göttingen

Gesellschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig, Tel.: (05 31) 70 08-1, Telex: 9-5 26 67

Vorsitzender des Aufsichtsrats:
Min. Dir. Dr. Friedrich Bischoff

Geschäftsführer:
Dr. Maria-Regina Kula
Dr. Helmut Zeitträger

Bankkonto:
Gebr. Lobbecke, Braunschweig
Konto 23 781 (BLZ 270 305 00)

Registriergericht:
Amtsgericht Braunschweig
HRB 477

ACKNOWLEDGEMENT OF RECEIPT AND ACCEPTANCE

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikroorganismen.

Name and address
of depositor:

BIOGEN N.V.
24 Handelskad
Willemsted,
Curacao, Netherland Antilles

Identification reference of
the microorganism used by
the depositor:

HFIF-G
M5219 (G-pPlc-HFIF-67-8)

Taxonomic designation of
the microorganism provi-
ded by the depositor:

Escherichia coli

DSM accession number of
the microorganism:

DSM 1854

Date of receipt of the
viable microorganism:

June 5, 1980

In addition to the identification reference and the taxonomic designation the depositor ~~has~~ ~~not~~ / has not provided a scientific description of the microorganism.

- ☒ The microorganism has been sent to the DSM directly by the depositor.
☐ The microorganism has been sent to the DSM on behalf of the depositor by the following depository under the designation and accession number given:

As stated by the depositor the microorganism may be rendered accessible to any third party under the following conditions:

- ☐ without any restrictions
☒ according to Rule 28 EPC and to the agreement between the European Patent Organisation and the DSM (Official Journal EPO 5, 301-307, 1978) and/or
☒ according to the Swedish patent legislation and to the agreement between the Swedish Patent Office and the DSM (Svensk Patenttidsning nr 12, 1979)
☒ in accordance with the "Declaration of Release" to be filed by the depositor with the DSM and the German Patent Office (at present Form P 2570)
☒ in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14) and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of America and b) without any restriction on availability to the public of the culture upon granting of a United States patent wherein the deposited microorganism is part of the disclosure of the invention
☒ in accordance with the French patent law
☐ in accordance with the conditions as specified by the depositor on enclosed separate sheet.

Göttingen, June 5, 1980

Place

date

DEUTSCHE SAMMLUNG VON MIKROORGANISMEN

der

Signature

Gesellschaft für Biotechnologische Forschung mbH
Grisebachstraße 8
D-3400 Göttingen

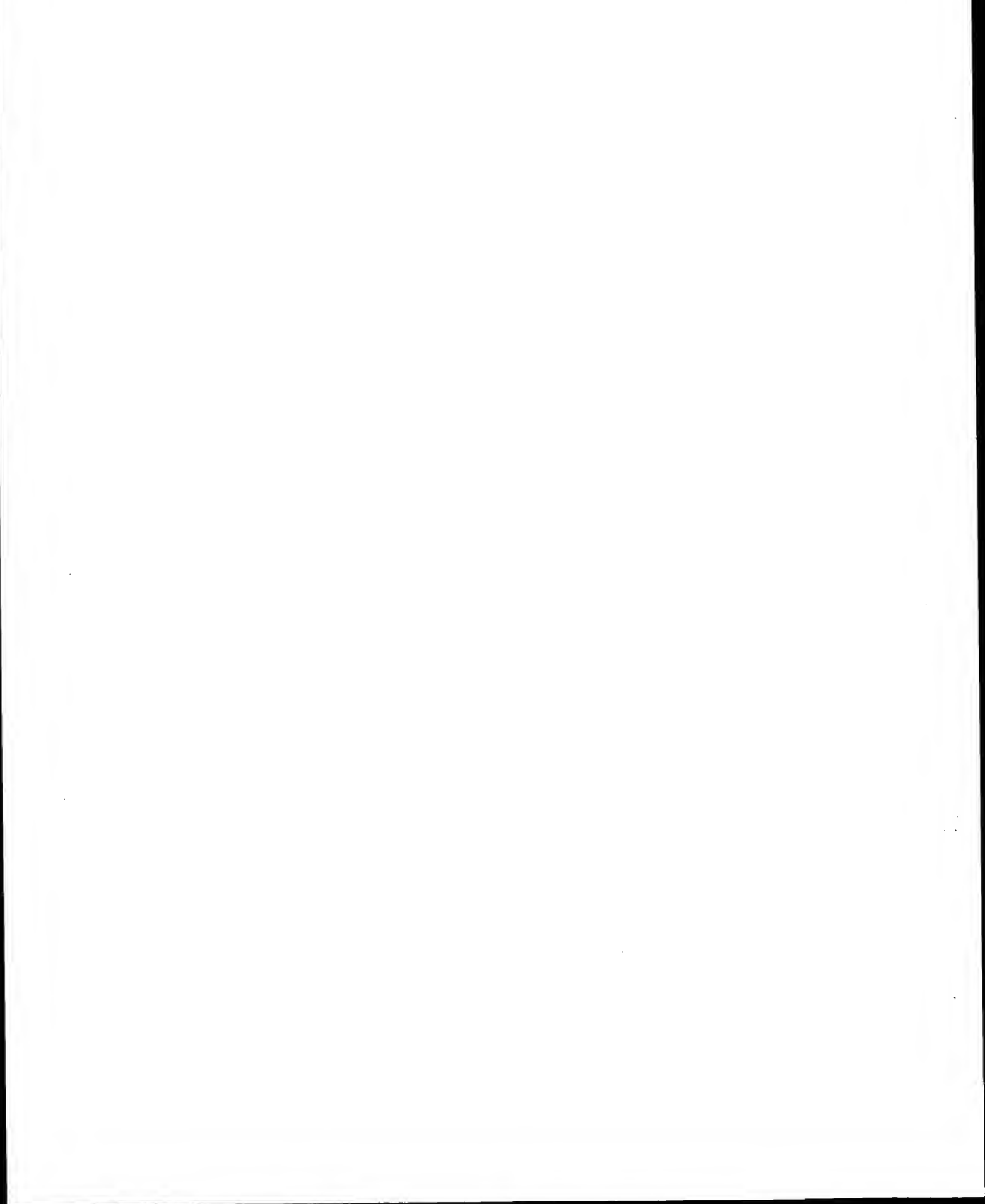
Gesellschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig. Tel: (05 31) 70 08-1, Telex: 9-5 28 87

Vorsitzender des Aufsichtsrats:
Min. Dir. Dr. Friedrich Bischoff

Geschäftsführer:
Dr. Maria-Regina Kula
Dr. Helmut Zeiträger

Bankkonto:
Gebr. Lohmecke, Braunschweig
Konto 23 781 (BLZ 270 305 00)

Registergericht:
Amtsgericht Braunschweig
HRB 477



RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3
AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2
To: (Name and Address of Depositor or Attorney)

James F. Haley, Jr., Ivor R. Elrifi
Fish & Neave
875 Third Avenue
New York, NY 10022

Deposited on Behalf of: Biogen, Inc. (Docket B8/B8 C 1P)

Identification Reference by Depositor:

ATCC Designation

<u>Escherichia coli</u> M5219 (G-pPLA-HFIF-67-12deltaMI), HFIF-H	31824
<u>Escherichia coli</u> HB101 (p[325]-qHFIF-4), HFIF-I	31825

The deposits were accompanied by: ____ a scientific description X a proposed taxonomic description indicated above.

The deposits were received February 26, 1981 by this International Depository Authority and have been accepted. A request to convert the deposits to a deposit under the Budapest Treaty was received on October 23, 1991.

AT YOUR REQUEST:

X We will inform you of requests for the strains for 30 years.

The strains will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strains.

If the cultures should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace them with living cultures of the same.

The strains will be maintained for a period of at least 30 years after the date of deposit, and for a period of at least five years after the most recent request for a sample. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the cultures cited above was tested October 25, 1991. On that date, the cultures were viable.

International Depository Authority: American Type Culture Collection, Rockville, Md. 20852 USA

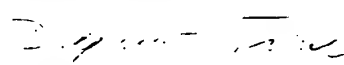
Signature of person having authority to represent ATCC:

Bobbie A. Brandon
Bobbie A. Brandon, Head, ATCC Patent Depository

Date: October 28, 1991

Biogen Inc.
14, Cambridge Center
Cambridge
Massachusetts
USA 02142


RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT
issued pursuant to Rule 7.1 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference given by the DEPOSITOR HFIF-A HB101 (G-pBR322 (Pst)/HFIF 3)	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY DSM 1791
II. SCIENTIFIC DESCRIPTION AND/OR TAXONOMIC DESIGNATION	
The microorganism identified under I. above was accompanied by: () a scientific description (X) a proposed taxonomic designation (Mark with a cross where applicable)	
III. RECEIPT AND ACCEPTANCE	
This International Depositary Authority accepts this microorganism identified under I. above, which was received by it on 1981-10-01 (Date of original deposit) ¹	
IV. RECEIPT OF REQUEST FOR CONVERSION	
The microorganism identified under I above was received by this International Depositary Authority on 1980-04-02 (date of original deposit) and a request to convert the original deposit to a deposit under the Budapest Treaty was received by it on 1991-10-24 (date of receipt of request for conversion).	
V. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSM-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Address: Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority, or of authorized official(s):  Date: 1991-10-28

¹ Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired

Biogen Inc.
14, Cambridge Center
Cambridge
Massachusetts
USA 02142

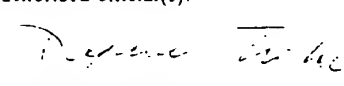
VIABILITY STATEMENT
issued pursuant to Rule 10.2 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

I. DEPOSITOR	II. IDENTIFICATION OF THE MICROORGANISM
<p>Name: Biogen Inc. 14, Cambridge Center Address: Cambridge Massachusetts USA 02142</p>	<p>Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 1791 Date of the deposit or of the transfer¹: 1981-10-01</p>
III. VIABILITY STATEMENT	
<p>The viability of the microorganism identified under II above was tested on 1989-07-07² On that date, the said microorganism was</p> <p>(X)³ viable ()³ no longer viable</p>	
IV. CONDITIONS UNDER WHICH THE VIABILITY TEST HAS BEEN PERFORMED ⁴	
IV. INTERNATIONAL DEPOSITARY AUTHORITY	
<p>Name: DSM DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Address: Mascheroder Weg 1 B D-3300 Braunschweig</p>	<p>Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):  Date: 1991-10-28</p>

- ¹ Indicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date (date of the new deposit or date of the transfer).
- ² In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.
- ³ Mark with a cross the applicable box.
- ⁴ Fill in if the information has been requested and if the results of the test were negative.

Biogen Inc.
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RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT
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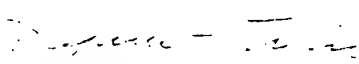
I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference given by the DEPOSITOR HFIF-B HB101(G-pBR322(Pst)/HFIF 6)	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 1792
II. SCIENTIFIC DESCRIPTION AND/OR TAXONOMIC DESIGNATION	
The microorganism identified under I. above was accompanied by: () a scientific description (X) a proposed taxonomic designation (Mark with a cross where applicable)	
III. RECEIPT AND ACCEPTANCE	
This International Depositary Authority accepts this microorganism identified under I. above, which was received by it on 1981-10-01 (Date of original deposit) ¹	
IV. RECEIPT OF REQUEST FOR CONVERSION	
The microorganism identified under I above was received by this International Depositary Authority on 1980-04-02 (date of original deposit) and a request to convert the original deposit to a deposit under the Budapest Treaty was received by it on 1991-10-24 (date of receipt of request for conversion).	
V. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSM-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Address: Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority, or of authorized official(s):  Date: 1991-10-28

¹ Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired

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VIABILITY STATEMENT

issued pursuant to Rule 10.2 by the
INTERNATIONAL DEPOSITARY AUTHORITY
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I. DEPOSITOR	II. IDENTIFICATION OF THE MICROORGANISM
Name: Biogen Inc. 14, Cambridge Center Address: Cambridge Massachusetts USA 02142	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 1792 Date of the deposit or of the transfer ¹ : 1981-10-01
III. VIABILITY STATEMENT	
The viability of the microorganism identified under II above was tested on 1989-07-07 ² On that date, the said microorganism was (X) ³ viable () ³ no longer viable	
IV. CONDITIONS UNDER WHICH THE VIABILITY TEST HAS BEEN PERFORMED ⁴	
IV. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSM DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Address: Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):  Date: 1991-10-28

¹ Indicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date (date of the new deposit or date of the transfer).

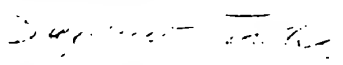
² In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.

³ Mark with a cross the applicable box.

⁴ Fill in if the information has been requested and if the results of the test were negative.

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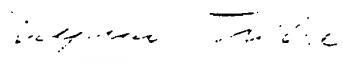
I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference given by the DEPOSITOR HFIF-C HB101(G-pBR322(Pst)/HFIF 7)	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 1793
II. SCIENTIFIC DESCRIPTION AND/OR TAXONOMIC DESIGNATION	
The microorganism identified under I. above was accompanied by: () a scientific description (X) a proposed taxonomic designation (Mark with a cross where applicable)	
III. RECEIPT AND ACCEPTANCE	
This International Depositary Authority accepts this microorganism identified under I. above, which was received by it on 1981-10-01 (Date of original deposit) ¹	
IV. RECEIPT OF REQUEST FOR CONVERSION	
The microorganism identified under I above was received by this International Depositary Authority on 1980-04-02 (date of original deposit) and a request to convert the original deposit to a deposit under the Budapest Treaty was received by it on 1991-10-24 (date of receipt of request for conversion).	
V. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSM-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Adress: Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):  Date: 1991-10-28

¹ Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired
Form DSM-BP/4 (sole page) 0291

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VIABILITY STATEMENT

issued pursuant to Rule 10.2 by the
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I. DEPOSITOR	II. IDENTIFICATION OF THE MICROORGANISM
Name: Biogen Inc. 14, Cambridge Center Address: Cambridge Massachusetts USA 02142	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY. DSM 1793 Date of the deposit or of the transfer ¹ 1981-10-01
III. VIABILITY STATEMENT	
The viability of the microorganism identified under II above was tested on 1989-07-07 ² On that date, the said microorganism was (X) ³ viable () ³ no longer viable	
IV. CONDITIONS UNDER WHICH THE VIABILITY TEST HAS BEEN PERFORMED ⁴	
IV. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSM DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Address: Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):  Date: 1991-10-28

¹ Indicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date (date of the new deposit or date of the transfer).

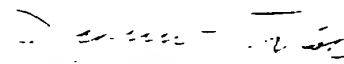
² In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.

³ Mark with a cross the applicable box.

⁴ Fill in if the information has been requested and if the results of the test were negative.

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RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT
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I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference given by the DEPOSITOR HFIF-D M5219 (G-pPLa-HFIF-67-12)	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 1851
II. SCIENTIFIC DESCRIPTION AND/OR TAXONOMIC DESIGNATION	
The microorganism identified under I. above was accompanied by: () a scientific description (X) a proposed taxonomic designation (Mark with a cross where applicable)	
III. RECEIPT AND ACCEPTANCE	
This International Depositary Authority accepts this microorganism identified under I. above, which was received by it on 1981-10-01 (Date of original deposit) ¹	
IV. RECEIPT OF REQUEST FOR CONVERSION	
The microorganism identified under I above was received by this International Depositary Authority on 1980-06-05 (date of original deposit) and a request to convert the original deposit to a deposit under the Budapest Treaty was received by it on 1991-10-24 (date of receipt of request for conversion).	
V. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSM-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Adress: Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):  Date: 1991-10-28

¹ Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired

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VIABILITY STATEMENT

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I. DEPOSITOR	II. IDENTIFICATION OF THE MICROORGANISM
Name: Biogen Inc. 14, Cambridge Center Address: Cambridge Massachusetts USA 02142	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 1851 Date of the deposit or of the transfer ¹ : 1981-10-01
III. VIABILITY STATEMENT	
The viability of the microorganism identified under II above was tested on 1990-11-29 ² On that date, the said microorganism was (X) ³ viable () ³ no longer viable	
IV. CONDITIONS UNDER WHICH THE VIABILITY TEST HAS BEEN PERFORMED ⁴	
IV. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSM DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Address: Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):  Date: 1991-10-28

¹ Indicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date (date of the new deposit or date of the transfer).

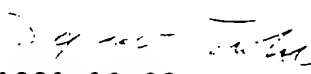
² In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.

³ Mark with a cross the applicable box.

⁴ Fill in if the information has been requested and if the results of the test were negative.

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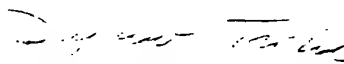
RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT
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I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference given by the DEPOSITOR HFIF-E K12 Δ HI (G-pPLa-HFIF-67-12)	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 1852
II. SCIENTIFIC DESCRIPTION AND/OR TAXONOMIC DESIGNATION	
The microorganism identified under I. above was accompanied by: () a scientific description (X) a proposed taxonomic designation (Mark with a cross where applicable)	
III. RECEIPT AND ACCEPTANCE	
This International Depositary Authority accepts this microorganism identified under I. above, which was received by it on 1981-10-01 (Date of original deposit) ¹	
IV. RECEIPT OF REQUEST FOR CONVERSION	
The microorganism identified under I above was received by this International Depositary Authority on 1980-06-05 (date of original deposit) and a request to convert the original deposit to a deposit under the Budapest Treaty was received by it on 1991-10-24 (date of receipt of request for conversion).	
V. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSM-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Address: Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):  Date: 1991-10-28

¹ Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired.

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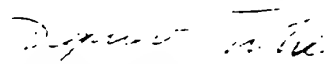
VIABILITY STATEMENT
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I. DEPOSITOR		II. IDENTIFICATION OF THE MICROORGANISM	
Name: Biogen Inc. 14, Cambridge Center Address: Cambridge Massachusetts USA 02142		Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 1852 Date of the deposit or of the transfer ¹ : 1981-10-01	
III. VIABILITY STATEMENT			
The viability of the microorganism identified under II above was tested on 1990-11-29 ² On that date, the said microorganism was (X) ³ viable () ³ no longer viable			
IV. CONDITIONS UNDER WHICH THE VIABILITY TEST HAS BEEN PERFORMED⁴			
IV. INTERNATIONAL DEPOSITARY AUTHORITY			
Name: DSM DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Address: Mascheroder Weg 1 B D-3300 Braunschweig		Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):  Date: 1991-10-28	

- ¹ Indicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date (date of the new deposit or date of the transfer).
- ² In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.
- ³ Mark with a cross the applicable box.
- ⁴ Fill in if the information has been requested and if the results of the test were negative.

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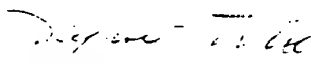
I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference given by the DEPOSITOR HFIF-F M5219 (G-pPLa-HFIF-67-12 Δ 19)	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 1853
II. SCIENTIFIC DESCRIPTION AND/OR TAXONOMIC DESIGNATION	
The microorganism identified under I. above was accompanied by: () a scientific description (X) a proposed taxonomic designation (Mark with a cross where applicable)	
III. RECEIPT AND ACCEPTANCE	
This International Depositary Authority accepts this microorganism identified under I. above, which was received by it on 1981-10-01 (Date of original deposit) ¹	
IV. RECEIPT OF REQUEST FOR CONVERSION	
The microorganism identified under I above was received by this International Depositary Authority on 1980-06-05 (date of original deposit) and a request to convert the original deposit to a deposit under the Budapest Treaty was received by it on 1991-10-24 (date of receipt of request for conversion).	
V. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSM-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Adress: Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):  Date: 1991-10-28

¹ Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired
Form DSM-BP/4 (sole page) 0291

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VIABILITY STATEMENT

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I. DEPOSITOR	II. IDENTIFICATION OF THE MICROORGANISM
Name: Biogen Inc. 14, Cambridge Center Address: Cambridge Massachusetts USA 02142	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 1853 Date of the deposit or of the transfer ¹ : 1981-10-01
III. VIABILITY STATEMENT	
The viability of the microorganism identified under II above was tested on 1990-11-29 ² On that date, the said microorganism was (X) ³ viable () ³ no longer viable	
IV. CONDITIONS UNDER WHICH THE VIABILITY TEST HAS BEEN PERFORMED ⁴	
IV. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSM DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Address: Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):  Date: 1991-10-28

¹ Indicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date (date of the new deposit or date of the transfer).

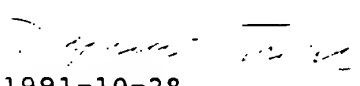
² In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.

³ Mark with a cross the applicable box.

⁴ Fill in if the information has been requested and if the results of the test were negative.

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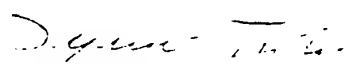
I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference given by the DEPOSITOR HFIF-G M5219 (G-pPlc-HFIF-67-8)	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY DSM 1854
II. SCIENTIFIC DESCRIPTION AND/OR TAXONOMIC DESIGNATION	
The microorganism identified under I. above was accompanied by: () a scientific description (X) a proposed taxonomic designation (Mark with a cross where applicable)	
III. RECEIPT AND ACCEPTANCE	
This International Depositary Authority accepts this microorganism identified under I. above, which was received by it on 1981-10-01 (Date of original deposit) ¹	
IV. RECEIPT OF REQUEST FOR CONVERSION	
The microorganism identified under I above was received by this International Depositary Authority on 1980-06-05 (date of original deposit) and a request to convert the original deposit to a deposit under the Budapest Treaty was received by it on 1991-10-24 (date of receipt of request for conversion).	
V. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSM-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Adress: Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):  Date: 1991-10-28

¹ Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired
Form DSM-BP/4 (sole page) 0291

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VIABILITY STATEMENT

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I. DEPOSITOR	II. IDENTIFICATION OF THE MICROORGANISM
Name: Biogen Inc. 14, Cambridge Center Address: Cambridge Massachusetts USA 02142	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 1854 Date of the deposit or of the transfer ¹ : 1981-10-01
III. VIABILITY STATEMENT	
The viability of the microorganism identified under II above was tested on 1990-03-27 ² On that date, the said microorganism was (X) ³ viable () ³ no longer viable	
IV. CONDITIONS UNDER WHICH THE VIABILITY TEST HAS BEEN PERFORMED ⁴	
IV. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSM DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Address: Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):  Date: 1991-10-28

¹ Indicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date (date of the new deposit or date of the transfer).

² In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.

³ Mark with a cross the applicable box.

⁴ Fill in if the information has been requested and if the results of the test were negative.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENTS

Examiner : J. Martinell
Group : 1805
Applicant : Walter C. Fiers
Serial No. : 387,503
Filed : July 28, 1989
For : DNA SEQUENCES, RECOMBINANT DNA MOLECULES AND
PROCESSES FOR PRODUCING HUMAN FIBROBLAST
INTERFERON-LIKE POLYPEPTIDES

New York, New York
June 3, 1994

DECLARATION OF JAMES F. HALEY, JR.

I, JAMES F. HALEY, JR., declare that:

1. I am the attorney of record in the above-identified patent application. I make this declaration to set forth the facts related to the deposit of microorganisms referred to on pages 94-95 of that application and to the permanence, availability and replacement of those cultures.

2. I identify the following documents that demonstrate the deposit of those microorganisms and the permanence, availability and replacement of those cultures:

Exhibit 1 -- True copies of (a) Deutsche Sammlung von Mikroorganismen "Acknowledgement of Receipt and Acceptance", dated April 2, 1980 for deposit HFIF-A (DSM 1791); (b) October 16, 1991 letter to the DSM with enclosures including a request to convert this deposit to a Budapest Treaty deposit; (c) Receipt of Request And Viability Statement from DSM confirming that this deposit has been converted to a Budapest Treaty deposit.

Exhibit 2 -- True copies of (a) Deutsche Sammlung von Mikroorganismen "Acknowledgement of Receipt and Acceptance", for culture HFIF-B (DSM 1792), dated April 2, 1980; (b) October 16, 1991 letter to the DSM with enclosures including a request to convert this deposit to a Budapest Treaty deposit; (c) Receipt of Request And Viability Statement from DSM confirming that this deposit has been converted to a Budapest Treaty deposit.

Exhibit 3 -- True copies of (a) Deutsche Sammlung von Mikroorganismen "Acknowledgement of Receipt and Acceptance", dated April 2, 1980, for culture HFIF-C (DSM 1793); (b) October 16, 1991 letter to the DSM with enclosures including a request to convert this deposit to a Budapest Treaty deposit; (c) Receipt of Request And Viability Statement from DSM confirming that this deposit has been converted to a Budapest Treaty deposit.

Exhibit 4 -- True copies of (a) Deutsche Sammlung von Mikroorganismen "Acknowledgement of Receipt and Acceptance" for culture HFIF-D (DSM 1851), dated June 5, 1980; (b) October 16, 1991 letter to the DSM with enclosures including a request to convert this deposit to a Budapest Treaty deposit; (c) Receipt of Request And Viability Statement from DSM confirming that this deposit has been converted to a Budapest Treaty deposit.

Exhibit 5 -- True copies of (a) Deutsche Sammlung von Mikroorganismen "Acknowledgement of Receipt and Acceptance" for culture HFIF-E (DSM 1852), dated June 5, 1980; (b) October 16, 1991 letter to the DSM with enclosures including a request to convert this deposit to a Budapest Treaty deposit; (c) Receipt of Request And Viability Statement from DSM confirming

that this deposit has been converted to a Budapest Treaty deposit.

Exhibit 6 -- True copies of (a) Deutsche Sammlung von Mikroorganismen "Acknowledgement of Receipt and Acceptance" for culture HFIF-F (DSM 1853), dated June 5, 1980; (b) October 16, 1991 letter to the DSM with enclosures including a request to convert this deposit to a Budapest Treaty deposit; (c) Receipt of Request And Viability Statement from DSM confirming that this deposit has been converted to a Budapest Treaty deposit.

Exhibit 7 -- True copies of (a) Deutsche Sammlung von Mikroorganismen "Acknowledgement of Receipt and Acceptance" for culture HFIF-G (DSM 1854), dated June 5, 1980; (b) October 16, 1991 letter to the DSM with enclosures including a request to convert this deposit to a Budapest Treaty deposit; (c) Receipt of Request And Viability Statement from DSM confirming that this deposit has been converted to a Budapest Treaty deposit; (d) April 28, 1994 letter from DSM with enclosures including a revised Receipt of Request for this deposit.

Exhibit 8 -- True copies of (a) American Type Culture Collection "Acknowledgement of Receipt and Acceptance" for cultures HFIF-H and HFIF-I (ATCC 31824, ATCC 31825), dated February 27, 1981; (b) October 16, 1991 letter to ATCC with enclosures including a request to convert these deposits to Budapest Treaty deposits; (c) Receipt of Request And Viability Statement from ATCC confirming that these deposits have been converted to Budapest Treaty deposits; (d) revised Receipt of Request from ATCC for these deposits, dated May 6, 1994.

3. On the bases of the above-identified exhibits, I am informed and believe that the deposits of microorganisms

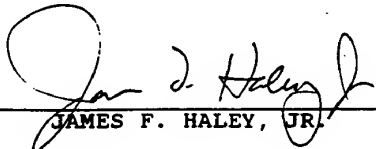
referred to on pages 94-95 of the above-identified application were made, have been converted to deposits under the Budapest Treaty On The International Recognition Of The Deposit Of Microorganisms For The Purposes Of Patent Procedure, and are being maintained under the applicable rules and regulations of that Treaty and of the United States Patent and Trademark Office as to their permanence, availability and replacement.

4. On the basis of Exhibit 7, I am informed and believe that the deposit papers referring to deposit DSM 1854 have been amended. In the amended papers, deposit DSM 1854 refers to strain Escherichia coli HFIF-G M5219 (G-pPLC-HFIF-67-8). Attached as part of Exhibit 7 is an April 28, 1994 letter from Dr. Vera Weihs of the DSM explaining this amendment, along with a copy of the amended Receipt form.

5. On the basis of Exhibit 8, I am informed and believe that the deposit papers referring to ATCC 31824 and ATCC 31825 have been amended. In the amended papers, deposit ATCC 31824 refers to strain Escherichia coli M5219 (G-pPLa-HFIF-67-12AMI) and deposit ATCC 31825 refers to strain Escherichia coli HB101 (p[325]-gHFIF4). Attached as part of Exhibit 8 is a May 6, 1994 amended Receipt from ATCC.

6. I am informed and believe that the applicant agrees to maintain the permanence of these deposits for the full enforceable term of any patent issuing from this application and to irrevocably remove all restrictions on the availability to the public of the material so deposited upon granting of a patent.

7. The undersigned declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such wilful false statements may jeopardize the validity of this application or any patent issuing thereon.


JAMES F. HALEY, JR.

Signed at New York, New York
this 3rd day of June, 1994

ACKNOWLEDGEMENT OF RECEIPT AND ACCEPTANCE

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikroorganismen.

Name and address
of depositor:

Biogen N.V.
24 Handelskad
Willemsted
Curacao, Netherland Antilles

Identification reference of
the microorganism used by
the depositor:

HFIF-A
HB101(G-pBR322(Pst)/HFIF 3)

Taxonomic designation of the microorganism provided by the depositor:

Escherichia coli

DSM accession number of
the microorganism:

DSM 1791

Date of receipt of the
viable microorganism:

April 2, 1980

In addition to the identification reference and the taxonomic designation the depositor ^{XXX} has ~~provided~~ / has not provided a scientific description of the microorganism.

- ☒ The microorganism has been sent to the DSM directly by the depositor.
- ☐ The microorganism has been sent to the DSM on behalf of the depositor by the following
depository under the designation and accession number given: —

As stated by the depositor the microorganism may be rendered accessible to any third party under the following conditions:

- ☐ without any restrictions
- ☒ according to Rule 28 EPC and to the agreement between the European Patent Organisation and the DSM (Official Journal EPO 5, 301-307, 1978) and/or
- ☒ according to the Swedish patent legislation and to the agreement between the Swedish Patent Office and the DSM (Svensk Patenttidning nr 12, 1979)
- ☒ in accordance with the "Declaration of Release" to be filed by the depositor with the DSM and the German Patent Office (at present Form P 2570)
- ☒ in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14) and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of America and b) without any restriction on availability to the public of the culture upon granting of a United States patent wherein the deposited microorganism is part of the disclosure of the invention
- ☒ in accordance with the French patent law
- ☐ in accordance with the conditions as specified by the depositor on enclosed separate sheet.

Göttingen, April 2, 1980

Place _____ date _____ **DEUTSCHE SAMMLUNG VON MIKROORGANISMEN** der _____ Signature _____

Gesellschaft für Biotechnologische Forschung mbH
Gnsbachstraße 8
D-3400 Göttingen

Gesellschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig, Tel.: (05 31) 70 08-1, Telex: 9-5 26 67

Vorsitzender des Aufsichtsrats:
Hr. Dr. Dr. Friedrich B. Scholl

Geschäftsführer:
Dr. Maria Regina Kula
Dr. Heimit Zellweger

Bankkonto
Geb. LÖbbecke, Brunnenstr. 1
Konto 23 761 (BLZ 25 0 0 0 0)

Registernummer:
Antragsteller: Braunschweig
NR 477

003-0979

FISH & NEAVE

875 THIRD AVENUE
NEW YORK, N.Y. 10022-6250

TELEPHONE: (212) 715-0800

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CABLE ADDRESS: FISHNEAVE

TELECOPIER: (212) 715-0874

October 16, 1991

CHARLES S. SMITH
DAVID W. BLUNT
ALBERT FET
JOHN O. THOMSON
HERBERT F. SCHWARTZ
LARRY I. KULLER
WILLIAM J. GILBERT
ERIC C. WOODSON
JOHN E. HATMAN
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NORMAN H. BEAMER
LEVIN J. CULLMAN
GLENN A. DUSTENHOLZ
SHARON PROBERT
BARBARA A. PRESH
RON E. SHALMAN
DOUGLAS J. GILBERT
DENISE L. LORING
JEFFREY H. HUBERMAN

FREDERICK P. FISH
1889-1890
CHARLES NEAVE
1887-1897

A. PETER ABLES

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CHRISTOPHER P. BOGZIELA

Deutsche Sammlung von Mikroorganismen
Und Zellkulturen GmbH
Mascheroder Weg 1b
D-3300 Braunschweig
Federal Republic of Germany

Biogen - B8/B8 CIP
Deposits DSM 1791-1793; 1851-1854

Dear Sir:

We have enclosed seven (7) applications to convert the above-identified deposits already deposited at the DSM into deposits under the Budapest Treaty. The DSM designations, as well as the strain designations given by the depositor, are identified on the application forms. In addition, we enclose copies of the "Acknowledgement of Receipt and Acceptance" forms for these deposits and the "Accession Form for Deposit" for DSM 1851-1854, containing the media and culture requirements. Please send your debit note for these conversions to my attention.

Please note that the original depositor has undergone a corporate name and address change from Biogen N.V., 24 Handelskad, Willemsted, Curacao, Netherland Antilles, to Biogen, Inc., 14 Cambridge Center, Cambridge, Massachusetts, U.S.A. 02142. This name and address change has been duly registered according to the national laws in the Patent Office of each country where a patent application has been filed referencing these deposits.

If you have any questions or require further information, please do not hesitate to contact us.

Thanks for your help.

Yours very truly,

James F. Haley, Jr.
Ivor R. Elrifi
Attorneys for Biogen, Inc.

JFH/IRE:bb
Enclosures

FOR THE PURPOSE OF PATENT PROCEDURE

STATEMENT IN THE CASE OF AN ORIGINAL DEPOSIT
pursuant to Rule 6.1

To
DEUTSCHE SAMMLUNG VON MICROORGANISMEN
UND ZELLKULTUREN GmbH
Mascheroder Weg 1b
D-3300 Braunschweig
Federal Republic of Germany

To be filled in by the Depository Authority

DSM-Accession number :

Date culture received :

BACTERIA/FUNGI¹

THE UNDERSIGNED HEREBY DEPOSITS UNDER THE BUDAPEST TREATY THE MICROORGANISM IDENTIFIED HEREUNDER AND UNDERTAKES NOT TO WITHDRAW THE DEPOSIT FOR THE PERIOD SPECIFIED IN RULE 9.1⁴

I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference ³ : HFIF-A HB101(G-pBR322(Pst)/HFIF 3) Taxonomic designation ⁴ : Escherichia coli	The culture to be deposited is : (X) a pure culture () a mixture of microorganisms (Mark with a cross where applicable)
II. CONDITIONS FOR CULTIVATION (X) ⁵	
Medium: as according to original deposit application for DSM 1791	pH before sterilisation : Sterilisation min at °C pH after sterilisation: Oxygen relationship : () aerobic () microaerophilic () obligate anaerobic Specific gaseous requirements : Incubation temperature: °C Incubation time: Short term storage at: °C Interval of transfer:

¹ The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsäuren" (5. überarbeitete Fassung BNFT)

² This form may also be used if the undersigned converts into a deposit under the Budapest Treaty the deposit of a microorganism that he or his predecessor in title has already deposited, outside the Budapest Treaty, with the same depository institution either before (Rule 6.4(d)) or after the acquisition by that institution of the status of international depository authority.

³ Number, symbols etc., given to the microorganism by the depositor.

⁴ It is strongly recommended that the taxonomic designation and/or scientific description (see under VII.) of the microorganism be indicated.

⁵ Mark with a cross if additional information is given on an attached sheet.

III. CONDITIONS FOR LONG TERM STORAGE	(X) ⁵
IV. CONDITIONS FOR TESTING VIABILITY	(X) ⁵
V. COMPONENTS OF MIXED CULTURES (WHEN APPLICABLE)	(X) ⁵
<p>Description of components:</p> <p>Method(s) for checking presence of components:</p> 	

⁵ Mark with a cross if additional information is given on an attached sheet.

VI. PROPERTIES DANGEROUS TO HEALTH OR ENVIRONMENT

Hazard group of the microorganisms named under I. according to DIN 58 956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9:¹

.....

THE STRAIN HAS TO BE HANDLED UNDER THE FOLLOWING LABORATORY CONTAINMENT LEVEL¹:

() L1 () L2
() L3 () L4

IS THIS STRAIN DANGEROUS TO HEALTH OR THE ENVIRONMENT ? () YES (X) NO
(if yes, please specify:) (X)⁵

(X) the undersigned is not aware of such properties

IF THE MICROORGANISM IS GENETICALLY MANIPULATED:

1. PLEASE INDICATE ALL THE RELEVANT GENETIC PROPERTIES:

general genetic recombination (rec):

sensitivities:

resistances:

modifications:

restrictions:

auxotrophies:

2. DESIGNATION OF THE DONOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE PLASMID:

3. If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKBS guidelines⁶ or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION).

1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINITELY HAVE NO PATHOGENIC POTENTIAL.

() YES

2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL.

() YES

IN THE LATTER CASE PLEASE NOTE:

According to the regulations of the ZKBS⁶ the DSM can only accept genetically manipulated, potentially pathogenic organisms for deposition when a copy of the permit issued by the ZKBS⁶ (or by an equivalent national biological safety commission) for work on the organisms accompanies the deposition form

¹ The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

⁵ Mark with a cross if additional information is given on an attached sheet.

⁶ ZKBS = Zentrale Kommission für Biologische Sicherheit (Central Commission for Biological Safety)

VIII. ADDITIONAL DATA

()⁸IX. DEPOSITOR⁹

Name: Biogen, Inc.

Signature:

James F. Haley, Jr.
Ivor R. Elrifi
James F. Haley, Jr.
Ivor R. Elrifi
Attorneys for Biogen, Inc.

Address: 14 Cambridge Center
Cambridge, Massachusetts 02142

Date:

Fish & Neave
875 Third Avenue
New York, New York 10022

10/18/91

⁵ Mark with a cross if additional information is given on an attached sheet.

⁷ It is strongly recommended that the scientific description and/or proposed taxonomic designation (see 1.) of the microorganism be indicated.

⁸ Mark with a cross if additional information (other than the information referred to in footnote 4 is given on an attached sheet, such as the source of the microorganism, the name(s) and the address(es) of any other depository institution(s) with which the microorganism has been deposited, or the criterion used when drafting the proposed taxonomic designation (The supplying of such information is optional).

⁹ The name of the depositor must be identical with the signature.

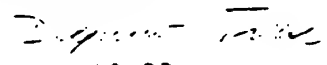
In case of a legal entity the signatures of two representatives, officially nominated by this entity, are required.

Where the signature is required on behalf of a legal entity, the typewritten name(s) of the natural person(s) signing on behalf of the legal entity should accompany the signature(s).

INTERNATIONAL FORM

Biogen Inc.
14, Cambridge Center
Cambridge
Massachusetts
USA 02142

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT
issued pursuant to Rule 7.1 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference given by the DEPOSITOR HFIF-A HB101 (G-pBR322 (Pst)/HFIF 3)	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 1791
II. SCIENTIFIC DESCRIPTION AND/OR TAXONOMIC DESIGNATION	
The microorganism identified under I. above was accompanied by: () a scientific description (X) a proposed taxonomic designation (Mark with a cross where applicable)	
III. RECEIPT AND ACCEPTANCE	
This International Depositary Authority accepts this microorganism identified under I. above, which was received by it on 1981-10-01 (Date of original deposit) ¹	
IV. RECEIPT OF REQUEST FOR CONVERSION	
The microorganism identified under I above was received by this International Depositary Authority on 1980-04-02 (date of original deposit) and a request to convert the original deposit to a deposit under the Budapest Treaty was received by it on 1991-10-24 (date of receipt of request for conversion).	
V. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSM-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Address: Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorised official(s):  Date: 1991-10-28

¹ Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired
Form DSM-BP/4 (sole page) 0291

RECOGNITION OF THE DEPOSIT OF MICROORGANISMS
FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

Biogen Inc.
14, Cambridge Center
Cambridge
Massachusetts
USA 02142

VIABILITY STATEMENT
issued pursuant to Rule 10.2 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

I. DEPOSITOR	II. IDENTIFICATION OF THE MICROORGANISM
Name: Biogen Inc. 14, Cambridge Center Address: Cambridge Massachusetts USA 02142	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY DSM 1791 Date of the deposit or of the transfer ¹ : 1981-10-01
III. VIABILITY STATEMENT	
The viability of the microorganism identified under II above was tested on 1989-07-07 ² On that date, the said microorganism was (X) ³ viable () ³ no longer viable	
IV. CONDITIONS UNDER WHICH THE VIABILITY TEST HAS BEEN PERFORMED ⁴	
IV. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSM DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Address: Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorised official(s): <i>Dieter T. K.</i> Date: 1991-10-28

- ¹ Indicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date (date of the new deposit or date of the transfer).
² In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.
³ Mark with a cross the applicable box.
⁴ Fill in if the information has been requested and if the results of the test were negative.

ACKNOWLEDGEMENT OF RECEIPT AND ACCEPTANCE

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikroorganismen.

Name and address
of depositor:

Biogen N.V.
24 Handelskad
Willemsted
Curacao, Netherland Antilles

Identification reference of
the microorganism used by
the depositor:

HFIF-8
HB101(G-pBR322(Pst))/HFIF 6)

Taxonomic designation of
the microorganism provi-
ded by the depositor:

Escherichia coli

DSM accession number of
the microorganism;

DSM 1792

Date of receipt of the
viable microorganism:

April 2, 1980

In addition to the identification reference and the taxonomic designation the depositor ~~has~~
~~has~~ has not provided a scientific description of the microorganism.

- ☒ The microorganism has been sent to the DSM directly by the depositor.
☐ The microorganism has been sent to the DSM on behalf of the depositor by the following
depository under the designation and accession number given: _____

As stated by the depositor the microorganism may be rendered accessible to any third party
under the following conditions:

- ☐ without any restrictions
☒ according to Rule 28 EPC and to the agreement between the European Patent Organisation
and the DSM (Official Journal EPD 5, 301-307, 1978) and/or
☒ according to the Swedish patent legislation and to the agreement between the Swedish
Patent Office and the DSM (Svensk Patenttiding nr 12, 1979)
☒ in accordance with the "Declaration of Release" to be filed by the depositor with the
DSM and the German Patent Office (at present Form P 2570)
in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14)
and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of
☒ America and b) without any restriction on availability to the public of the culture
upon granting of a United States patent wherein the deposited microorganism is part
of the disclosure of the invention
☒ in accordance with the French patent law
☐ in accordance with the conditions as specified by the depositor on enclosed separate
sheet.

Göttingen, April 2, 1980

Place date DEUTSCHE SAMMLUNG VON MIKROORGANISMEN
Signature
Gesellschaft für Biotechnologische Forschung mbH
Grisebachstrasse 8
D-3400 Göttingen

Gesellschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig, Tel.: (05 31) 70 08-1, Telex: 9-5 26 67

Vorsitzender des Aufsichtsrats:
Min. Dir. Dr. Friedrich Bischoff

Geschäftsführer:
Dr. Maria Regina Kula
Dr. Helmut Zeitträger

Bankkonto:
Gebr. Löbbecke, Braunschweig
Konto 23 781 (BLZ 270 305 00)

Registergericht:
Amtsgericht Brauns-
HB 477

003-0979

FISH & NEAVE
 '875 THIRD AVENUE
 NEW YORK, N.Y. 10022-6250

TELEPHONE (212) 715-0600
 TELEX 14-8367
 CABLE ADDRESS: FISHNEAVE
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October 16, 1991

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 DOUGLAS J. GILBERT
 DENNIS L. LEVINS
 JEFFREY H. HIGERMAN

FREDERICK R. FISH
 1889-1930
 CHARLES NEAVE
 1867-1937

A. PETER ABLES
 RICHARD A. HILL

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Deutsche Sammlung von Mikroorganismen
 Und Zellkulturen GmbH
 Mascheroder Weg 1b
 D-3300 Braunschweig
 Federal Republic of Germany

Biogen - B8/B8 CIP
Deposits DSM 1791-1793; 1851-1854

Dear Sir:

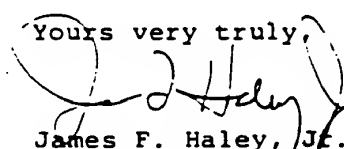
We have enclosed seven (7) applications to convert the above-identified deposits already deposited at the DSM into deposits under the Budapest Treaty. The DSM designations, as well as the strain designations given by the depositor, are identified on the application forms. In addition, we enclose copies of the "Acknowledgement of Receipt and Acceptance" forms for these deposits and the "Accession Form for Deposit" for DSM 1851-1854, containing the media and culture requirements. Please send your debit note for these conversions to my attention.

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If you have any questions or require further information, please do not hesitate to contact us.

Thanks for your help.

Yours very truly,


 James F. Haley, Jr.
 Ivor R. Elrifi
 Attorneys for Biogen, Inc.

JFH/IRE:bb
 Enclosures

RECOGNITION OF THE DEPOSIT OF MICRO¹ ISMS
FOR THE PURPOSE OF PATENT PROCEDURE

STATEMENT IN THE CASE OF AN ORIGINAL DEPOSIT
pursuant to Rule 6.1

To
DEUTSCHE SAMMLUNG VON MIKROORGANISMEN
UND ZELLKULTUREN GbR
Mascheroder Weg 1b
D-3300 Braunschweig
Federal Republic of Germany

To be filled in by the Depository Authority

DSM-Accession number :

Date culture received :

BACTERIA/FUNGI¹

THE UNDERSIGNED HEREBY DEPOSITS UNDER THE BUDAPEST TREATY THE MICROORGANISM IDENTIFIED HEREUNDER AND UNDERTAKES NOT TO WITHDRAW THE DEPOSIT FOR THE PERIOD SPECIFIED IN RULE 9.1²

I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference ³ : HFIF-B HB101(G-pBR322(Pst)/HFIF 6) Taxonomic designation ⁴ : Escherichia coli	The culture to be deposited is : (X) a pure culture () a mixture of microorganisms (Mark with a cross where applicable)
II. CONDITIONS FOR CULTIVATION (X) ⁵	
Medium: as according to original deposit application for DSM 1792	pH before sterilisation : Sterilisation min at °C pH after sterilisation: Oxygen relationship : () aerobic () microaerophilic () obligate anaerobic Specific gaseous requirements : Incubation temperature: °C Incubation time: Short term storage at: °C Interval of transfer:

¹ The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neu kombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

² This form may also be used if the undersigned converts into a deposit under the Budapest Treaty the deposit of a microorganism that he or his predecessor in title has already deposited, outside the Budapest Treaty, with the same depository institution either before (Rule 6.4(d)) or after the acquisition by that institution of the status of international depository authority.

³ Number, symbols etc., given to the microorganism by the depositor.

⁴ It is strongly recommended that the taxonomic designation and/or scientific description (see under VII.) of the microorganism be indicated.

⁵ Mark with a cross if additional information is given on an attached sheet.

III. CONDITIONS FOR LONG TERM STORAGE

(X)⁵

IV. CONDITIONS FOR TESTING VIABILITY

(X)⁵

V. COMPONENTS OF MIXED CULTURES (WHEN APPLICABLE)

(X)⁵

Description of components:

Method(s) for checking presence of components:

⁵ Mark with a cross if additional information is given on an attached sheet.

VI. PROPERTIES DANGEROUS TO HEALTH OR ENVIRONMENT

Hazard group of the microorganisms named under I. according to DIN 58 956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9:¹

.....

THE STRAIN HAS TO BE HANDLED UNDER THE FOLLOWING LABORATORY CONTAINMENT LEVEL¹:

- () L1 () L2
() L3 () L4

IS THIS STRAIN DANGEROUS TO HEALTH OR THE ENVIRONMENT ? () YES (X) NO
(if yes, please specify:) (X)⁵

(X) the undersigned is not aware of such properties

IF THE MICROORGANISM IS GENETICALLY MANIPULATED:

1. PLEASE INDICATE ALL THE RELEVANT GENETIC PROPERTIES:

general genetic recombination (rec):

sensitivities:

resistances:

modifications:

restrictions:

auxotrophies:

2. DESIGNATION OF THE DONOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE PLASMID:

3. If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKBS guidelines⁶ or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION).

1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINITELY HAVE NO PATHOGENIC POTENTIAL.

() YES

2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL.

() YES

IN THE LATTER CASE PLEASE NOTE:

According to the regulations of the ZKBS⁶ the DSM can only accept genetically manipulated, potentially pathogenic organisms for deposition when a copy of the permit issued by the ZKBS⁶ (or by an equivalent national biological safety commission) for work on the organisms accompanies the deposition form

¹ The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro rekombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

⁵ Mark with a cross if additional information is given on an attached sheet.

⁶ ZKBS = Zentrale Kommission für Biologische Sicherheit (Central Commission for Biological safety)

INTERNATIONAL FORM

Biogen Inc.
14, Cambridge Center
Cambridge
Massachusetts
USA 02142

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT
issued pursuant to Rule 7.1 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

I. IDENTIFICATION OF THE MICROORGANISM

Identification reference given by the DEPOSITOR

HFIF-B

HB101 (G-pBR322 (Pst)/HFIF 6)

Accession number given by the
INTERNATIONAL DEPOSITARY AUTHORITY

DSM 1792

II. SCIENTIFIC DESCRIPTION AND/OR TAXONOMIC DESIGNATION

The microorganism identified under I. above was accompanied by:

() a scientific description

(X) a proposed taxonomic designation

(Mark with a cross where applicable)

III. RECEIPT AND ACCEPTANCE

This International Depositary Authority accepts this microorganism identified under I. above, which was received by it
on 1981-10-01 (Date of original deposit)¹

IV. RECEIPT OF REQUEST FOR CONVERSION

The microorganism identified under I above was received by this International Depositary Authority on 1980-04-02
(date of original deposit) and a request to convert the original deposit to a deposit under the Budapest Treaty was
received by it on 1991-10-24 (date of receipt of request for conversion).

V. INTERNATIONAL DEPOSITARY AUTHORITY

Name: DSM-DEUTSCHE SAMMLUNG VON
MIKROORGANISMEN UND ZELLKULTUREN GmbH

Address: Mascheroder Weg 1 B
D-3300 Braunschweig

Signature(s) of person(s) having the power
to represent the International Depositary Authority,
or of authorised official(s):

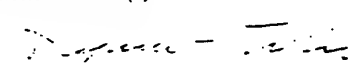
Date: 1991-10-28

¹ Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired

INTERNATIONAL FORM

Biogen Inc.
14, Cambridge Center
Cambridge
Massachusetts
USA 02142

VIABILITY STATEMENT
issued pursuant to Rule 10.2 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

I. DEPOSITOR		II. IDENTIFICATION OF THE MICROORGANISM	
Name: Biogen Inc. 14, Cambridge Center Address: Cambridge Massachusetts USA 02142		Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY DSM 1792 Date of the deposit or of the transfer ¹ : 1981-10-01	
III. VIABILITY STATEMENT			
The viability of the microorganism identified under II above was tested on 1989-07-07 ² On that date, the said microorganism was (X) ³ viable () ³ no longer viable			
IV. CONDITIONS UNDER WHICH THE VIABILITY TEST HAS BEEN PERFORMED ⁴			
IV. INTERNATIONAL DEPOSITARY AUTHORITY			
Name: DSM DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Address: Mascheroder Weg 1 B D-3300 Braunschweig		Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):  Date: 1991-10-28	

- ¹ Indicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date (date of the new deposit or date of the transfer).
² In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.
³ Mark with a cross the applicable box.
⁴ Fill in if the information has been requested and if the results of the test were negative.

GESELLSCHAFT FÜR BIOTECHNOLOGISCHE FORSCHUNG MBH

DSM · Grisebachstrasse 8 · D-3400 Göttingen, Germany

Tel. (05 51) 39 38 22 / 39 38 23

ACKNOWLEDGEMENT OF RECEIPT AND ACCEPTANCE

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikroorganismen.

Name and address
of depositor:

Biogen N.V.
24 Handelskad
Willemsted
Curacao, Netherland Antilles

Identification reference of
the microorganism used by
the depositor:

HFIF-C
HB101(G-pBR322(Pst))/HFIF 7)

Taxonomic designation of
the microorganism provi-
ded by the depositor:

Escherichia coli

DSM accession number of
the microorganism:

DSM 1793

Date of receipt of the
viable microorganism:

April 2, 1980

In addition to the identification reference and the taxonomic designation the depositor ^{XXX}has provided / has not provided a scientific description of the microorganism. ^{XXX}

- ☒ The microorganism has been sent to the DSM directly by the depositor.
☐ The microorganism has been sent to the DSM on behalf of the depositor by the following depository under the designation and accession number given:

As stated by the depositor the microorganism may be rendered accessible to any third party under the following conditions:

- ☐ without any restrictions
☒ according to Rule 28 EPC and to the agreement between the European Patent Organisation and the DSM (Official Journal EPO 2, 301-307, 1978) and/or
☒ according to the Swedish patent legislation and to the agreement between the Swedish Patent Office and the DSM (Svensk Patenttidning nr 12, 1979)
☒ in accordance with the "Declaration of Release" to be filed by the depositor with the DSM and the German Patent Office (at present Form P 2570)
☒ in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14) and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of America and b) without any restriction on availability to the public of the culture upon granting of a United States patent wherein the deposited microorganism is part of the disclosure of the invention
☒ in accordance with the French patent law
☐ in accordance with the conditions as specified by the depositor on enclosed separate sheet.

Göttingen, April 2, 1980

Place date DEUTSCHE SAMMLUNG VON MIKROORGANISMEN
der
Gesellschaft für Biotechnologische Forschung mbH
Grisebachstrasse 8
D-3400 Göttingen

Gesellschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig. Tel.: (05 31) 70 06-1, Telex: 9-S 26 67

Vorsitzender des Aufsichtsrats:
Min. Dir. Dr. Friedrich Bischoff

Geschäftsführer:
Dr. Maria-Regina Kula
Dr. Helmut Zeitträger

Bankkonto:
Gebr. Löbbecke, Braunschweig
Konto 23 781 (BLZ 270 305 00)

Registriergericht:
Amtsgericht Braun-
sweig 477

003-0979

FISH & NEA E

875 THIRD AVENUE
NEW YORK, N.Y. 10022-6250

TELEPHONE (212) 715-0600
TELEX 14-8367
CABLE ADDRESS: FISHNEAVE
TELECOPIER (212) 715-0674

October 16, 1991

CHARLES B. SMITH
DAVID W. PLANT
ALBERT FET
JOHN D. THOMSON
HERBERT F. SCHWARTZ
LARS I. ELLERSEID
WILLIAM J. GILBERT
ERIC C. WOOLSON
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EDWARD F. MULLOWNE
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RICHARD N. BARNES
LAURENCE S. ROGERS
THOMAS L. BARNETT
VINCENT N. PALLADINO
ROBERT J. GOLDMAN
THOMAS L. SECRET
DANIEL M. GANTY
NORMAN H. BEAMAN
KEVIN J. CULLIGAN
GLENN A. QUITEBOUT
SUSAN PRODOFF
MARGARET A. PIERRE
RON E. SHULMAN
DOUGLAS J. SILBERT
DENISE L. LORING
JEFFREY N. INGERMAN

FREDERICK P. FISH
1899-1930
CHARLES REAVE
1867-1937

A. PETER ADLER
RICHARD A. INZ

THOMAS J. VETTER

C. JOSEPH LAUSON II
LISA E. CRISTAL
EDWARD N. KELLY
MARK N. BLOOMBERG
ALAN D. SMITH
DAVID C. PLACHE
JANE A. HARRARD
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MITCHELL N. BROOKS
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EDWARD J. DI FRANCO
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MARK D. ENGELMANN
ERIC N. HUBBARD
DAVID A. LOEWENSTEIN
JOHN J. CASSINERIAN
LINDA A. WADLER
KELSEY I. NIX
MARTY E. GROES
JOHN W. HUNT
JOHN S. STORELLA
WILLIAM J. MC CASE
JOHN N. DESMARIS
VICKIE VEENEN
LESLIE A. MEDONELL
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KRISTINA MACKEY
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JOHN N. MATTHEWS
DONALD A. REED
SABRIELE E. KOSINS
JENNIFER M. HALL
DONALD L. SHADDS
ELIZABETH M. ALDRIDGE
CLAY WILSON
BRENDA J. PANICH
JEREMY LACH
EVAN N. BELL
JAMES F. BERON
DONALD A. KRASHOW
JEFFREY M. REES
LIANNA C. RALMAN
BRADFORD I. FRIEDMAN
DEBRA A. SCHTEMPO
LORETTA A. MIRAGLIA
MOREY WILDES
CHRISTOPHER J. HARNETT
MARIE H. MARICHEL
WILLIAM A. SCHNEIDER

Deutsche Sammlung von Mikroorganismen
Und Zellkulturen GmbH
Mascheroder Weg 1b
D-3300 Braunschweig
Federal Republic of Germany

Biogen - B8/B8 CIP
Deposits DSM 1791-1793; 1851-1854

Dear Sir:

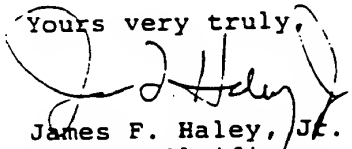
We have enclosed seven (7) applications to convert the above-identified deposits already deposited at the DSM into deposits under the Budapest Treaty. The DSM designations, as well as the strain designations given by the depositor, are identified on the application forms. In addition, we enclose copies of the "Acknowledgement of Receipt and Acceptance" forms for these deposits and the "Accession Form for Deposit" for DSM 1851-1854, containing the media and culture requirements. Please send your debit note for these conversions to my attention.

Please note that the original depositor has undergone a corporate name and address change from Biogen N.V., 24 Handelskad, Willemsted, Curacao, Netherland Antilles, to Biogen, Inc., 14 Cambridge Center, Cambridge, Massachusetts, U.S.A. 02142. This name and address change has been duly registered according to the national laws in the Patent Office of each country where a patent application has been filed referencing these deposits.

If you have any questions or require further information, please do not hesitate to contact us.

Thanks for your help.

Yours very truly,


James F. Haley, Jr.
Ivor R. Elrifi
Attorneys for Biogen, Inc.

JFH/IRE:bb
Enclosures

RECOGNITION OF THE DEPOSIT OF MICROORGANISMS
FOR THE PURPOSE OF PATENT PROCEDURE

STATEMENT IN THE CASE OF AN ORIGINAL DEPOSIT
pursuant to Rule 6.1

To
DEUTSCHE SAMMLUNG VON MICROORGANISMEN
UND ZELLKULTUREN GMBH
Mascheroder Weg 1b
D-3300 Braunschweig
Federal Republic of Germany

To be filled in by the Depositary Authority

DSM-Accession number :

Date culture received :

BACTERIA/FUNGI¹

THE UNDERSIGNED HEREBY DEPOSITS UNDER THE BUDAPEST TREATY THE MICROORGANISM IDENTIFIED HEREUNDER AND UNDERTAKES NOT TO WITHDRAW THE DEPOSIT FOR THE PERIOD SPECIFIED IN RULE 9.1²

I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference ³ : HFIF-C HB101(G-pBR322(Pst)/HFIF 7) Taxonomic designation ⁴ : Escherichia coli	The culture to be deposited is : (X) a pure culture () a mixture of microorganisms (Mark with a cross where applicable)
II. CONDITIONS FOR CULTIVATION () ⁵	
Medium: as according to original deposit application for DSM 1793	pH before sterilisation : Sterilisation min at °C pH after sterilisation: Oxygen relationship : () aerobic () microaerophilic () obligate anaerobic Specific gaseous requirements : Incubation temperature: °C Incubation time: Short term storage at: °C Interval of transfer:

¹ The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

² This form may also be used if the undersigned converts into a deposit under the Budapest Treaty the deposit of a microorganism that he or his predecessor in title has already deposited, outside the Budapest Treaty, with the same depositary institution either before (Rule 6.4(d)) or after the acquisition by that institution of the status of international depositary authority.

³ Number, symbols etc., given to the microorganism by the depositor.

⁴ It is strongly recommended that the taxonomic designation and/or scientific description (see under VII.) of the microorganism be indicated.

⁵ Mark with a cross if additional information is given on an attached sheet.

III. CONDITIONS FOR LONG TERM STORAGE

(X)⁵

IV. CONDITIONS FOR TESTING VIABILITY

(X)⁵

V. COMPONENTS OF MIXED CULTURES (WHEN APPLICABLE)

(X)⁵

Description of components:

Method(s) for checking presence of components:

⁵ Mark with a cross if additional information is given on an attached sheet.

VI. PROPERTIES DANGEROUS TO HEALTH OR ENVIRONMENT

Hazard group of the microorganisms, named under I. according to DIN 58 956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9:

THE STRAIN HAS TO BE HANDLED UNDER THE FOLLOWING LABORATORY CONTAINMENT LEVEL¹:

() L1

() L2

() L3

() L4

IS THIS STRAIN DANGEROUS TO HEALTH OR THE ENVIRONMENT ?

() YES

(X) NO

(if yes, please specify:)

(X)⁵

(X) the undersigned is not aware of such properties.

IF THE MICROORGANISM IS GENETICALLY MANIPULATED:

1. PLEASE INDICATE ALL THE RELEVANT GENETIC PROPERTIES:

general genetic recombination (rec):

sensitivities:

resistances:

modifications:

restrictions:

auxotrophies:

2. DESIGNATION OF THE DONOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE PLASMID:

3. If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKBS guidelines⁶ or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION).

1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINITELY HAVE NO PATHOGENIC POTENTIAL.

() YES

2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL.

() YES

IN THE LATTER CASE PLEASE NOTE:

According to the regulations of the ZKBS⁶ the DSM can only accept genetically manipulated, potentially pathogenic organisms for deposition when a copy of the permit issued by the ZKBS⁶ (or by an equivalent national biological safety commission) for work on the organisms accompanies the deposition form.

¹ The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neu kombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

⁵ Mark with a cross if additional information is given on an attached sheet.

⁶ ZKBS = Zentrale Kommission für Biologische Sicherheit (Central Commission for Biological safety)

VII. SCIENTIFIC DE.

ATION⁷(X)⁵

VIII. ADDITIONAL DATA

()⁸IX. DEPOSITOR⁹

Name: Biogen, Inc.

Signature:

James F. Haley, Jr.
Ivor R. Elrifi
Attorneys for Biogen, Inc.
Fish & Neave
875 Third Avenue
New York, New York 10022

Address: 14 Cambridge Center
Cambridge, Massachusetts
02142

Date:

12/18/91

⁵ Mark with a cross if additional information is given on an attached sheet.

⁷ It is strongly recommended that the scientific description and/or proposed taxonomic designation (see 1.) of the microorganism be indicated.

⁸ Mark with a cross if additional information (other than the information referred to in footnote 4 is given on an attached sheet, such as the source of the microorganism, the name(s) and the address(es) of any other depository institution(s) with which the microorganism has been deposited, or the criterion used when drafting the proposed taxonomic designation (The supplying of such information is optional).

⁹ The name of the depositor must be identical with the signature.

In case of a legal entity the signatures of two representatives, officially nominated by this entity, are required.

Where the signature is required on behalf of a legal entity, the typewritten name(s) of the natural person(s) signing on behalf of the legal entity should accompany the signature(s).

INTERNATIONAL FORM

Biogen Inc.
14, Cambridge Center
Cambridge
Massachusetts
USA 02142

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT
issued pursuant to Rule 7.1 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

I. IDENTIFICATION OF THE MICROORGANISM

Identification reference given by the DEPOSITOR

HFIF-C

HB101 (G-pBR322 (Pst)/HFIF 7)

Accession number given by the
INTERNATIONAL DEPOSITARY AUTHORITY

DSM 1793

II. SCIENTIFIC DESCRIPTION AND/OR TAXONOMIC DESIGNATION

The microorganism identified under I. above was accompanied by:

- () a scientific description
(X) a proposed taxonomic designation

(Mark with a cross where applicable)

III. RECEIPT AND ACCEPTANCE

This International Depositary Authority accepts this microorganism identified under I. above, which was received by it
on 1981-10-01 (Date of original deposit)¹

IV. RECEIPT OF REQUEST FOR CONVERSION

The microorganism identified under I above was received by this International Depositary Authority on 1980-04-02
(date of original deposit) and a request to convert the original deposit to a deposit under the Budapest Treaty was
received by it on 1991-10-24 (date of receipt of request for conversion).

V. INTERNATIONAL DEPOSITARY AUTHORITY

Name: DSM-DEUTSCHE SAMMLUNG VON
MIKROORGANISMEN UND ZELLKULTUREN GmbH

Address: Mascheroder Weg 1 B
D-3300 Braunschweig

Signature(s) of person(s) having the power
to represent the International Depositary Authority
or of authorised official(s):

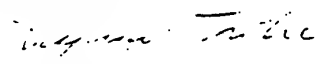
Date: 1991-10-28

¹ Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired

INTERNATIONAL FORM

Biogen Inc.
14, Cambridge Center
Cambridge
Massachusetts
USA 02142

VIABILITY STATEMENT
issued pursuant to Rule 10.2 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

I. DEPOSITOR	II. IDENTIFICATION OF THE MICROORGANISM
Name: Biogen Inc. 14, Cambridge Center Address: Cambridge Massachusetts USA 02142	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY DSM 1793 Date of the deposit or of the transfer ¹ 1981-10-01
III. VIABILITY STATEMENT	
The viability of the microorganism identified under II above was tested on 1989-07-07 ² On that date, the said microorganism was (X) ³ viable () ³ no longer viable	
IV. CONDITIONS UNDER WHICH THE VIABILITY TEST HAS BEEN PERFORMED ⁴	
IV. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSM DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Address: Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):  Date: 1991-10-28

- ¹ Indicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date (date of the new deposit or date of the transfer).
- ² In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.
- ³ Mark with a cross the applicable box.
- ⁴ Fill in if the information has been requested and if the results of the test were negative.

GESELLSCHAFT FÜR BIOTECHNOLOGISCHE FORSCHUNG MBH

DSM - Grisebachstrasse 8 · D-3400 Göttingen, Germany

Tel. (05 51) 39 38 22 / 39 38 23

ACKNOWLEDGEMENT OF RECEIPT AND ACCEPTANCE

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikroorganismen.

Name and address
of depositor:

BIOGEN N.V.
24 Handelskad
Willemsted,
Curacao, Netherland Antilles

Identification reference of
the microorganism used by
the depositor:

HFIF-D
M5219 (G-pPLa-HFIF-67-12)

Taxonomic designation of
the microorganism provided
by the depositor:

Escherichia coli

DSM accession number of
the microorganism:

DSM 1851

Date of receipt of the
viable microorganism:

June 5, 1980

In addition to the identification reference and the taxonomic designation the depositor ~~has~~
~~not~~ / has not provided a scientific description of the microorganism.

- ☐ The microorganism has been sent to the DSM directly by the depositor.
☐ The microorganism has been sent to the DSM on behalf of the depositor by the following
depository under the designation and accession number given: —

As stated by the depositor the microorganism may be rendered accessible to any third party
under the following conditions:

- ☐ without any restrictions
☒ according to Rule 28 EPC and to the agreement between the European Patent Organisation
and the DSM (Official Journal EPD 5, 301-307, 1978) and/or
☒ according to the Swedish patent legislation and to the agreement between the Swedish
Patent Office and the DSM (Svensk Patenttidning nr 12, 1979)
☒ in accordance with the "Declaration of Release" to be filed by the depositor with the
DSM and the German Patent Office (at present Form P 2570)
in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14)
and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of
☒ America and b) without any restriction on availability to the public of the culture
upon granting of a United States patent wherein the deposited microorganism is part
of the disclosure of the invention
☒ in accordance with the French patent law
☐ in accordance with the conditions as specified by the depositor on enclosed separate
sheet.

Göttingen, June 5, 1980

Place

date

DEUTSCHE SAMMLUNG VON MIKROORGANISMEN

der

Gesellschaft für Biotechnologische Forschung mbH

Grisebachstrasse 8

D-3400 Göttingen

Signature

Gesellschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig, Tel.: (05 31) 70 08-1, Telex: 9-5 25 67

Vorsitzender des Aufsichtsrats:
Min. Dir. Dr. Friedrich Bischoff

Geschäftsführer:
Dr. Maria Regina Kula
Dr. Helmut Zeitträger

Bankkonto:
Gebr. Lohbeck, Braunschweig
Konto 23 781 (BLZ 270 305 00)

Registergericht:
Amtsgericht Braunschweig
HRB 477

003-0979

ACCESSION: 1 for
deposition of patent microorganisms

DSM accession number: DSM 1251
Date culture received: 5 June 1980

The microorganism mentioned below is to be deposited with the DSM on account of
a patent application (to be) filed with

The deposit is made in accordance with Rule 28 EPC / with the Swedish patent legislation
(delete, if not applicable)

Name and address of depositor:

BIOGEN N.V.
24 Handelskad
Willemsted
Curacao, Netherland Antilles

Identification reference of the
microorganism given by the depo-
sitor (strain number, symbols etc.):

HFIF-D
M 5219 (G-p PL2 - HFIF-67-12)

Taxonomic designation of the
microorganism:

E. coli

A scientific description of the microorganism is attached on a separate sheet:

YES ☐

NO ☒

The microorganism to be deposited is

a pure culture

YES ☒

NO ☐

a mixture of strains:

YES ☐

NO ☒

In case of a mixed culture, please give a concise description on a separate sheet about the
components and methods to determine their viability.

Does the microorganism and/or its metabolic products present any hazard for man, animals,
plants or the environment: (if any, please specify on a separate sheet):

YES ☐

NO ☒

hand delivered

☒ The microorganism will be ~~sent~~ to the DSM directly by the depositor.

☐ The microorganism will be sent to the DSM on behalf of the depositor by
the following depository under the designation and accession number given:

The microorganism may be rendered accessible after receipt and deposition to any third party

☐ without any restriction

☒ according to Rule 28 EPC and to the agreement between the European Patent Organisation
and the DSM (Official Journal EPO 2, 301-307, 1978) and/or

☒ according to the Swedish patent legislation and to the agreement between the Swedish
Patent Office and the DSM (Svensk Patenttidning nr 12, 1979)

☒ in accordance with the "Declaration of Release" to be filed by the depositor with the
DSM and the German Patent Office (at present Form 2750)

☒ in accordance with a) Title 37, Code of Federal Regulations, Section 1.14 (37.CFR 1.14)
and Title 35, United States Code section 122 (35 U.S.C. 122) of the United States of
America and b) without any restrictions on the availability to the public of the culture
upon granting of the United States patent wherein the deposited microorganism is part
of the disclosure of the invention

☒ in accordance with the French patent law

☐ in accordance with the conditions as specified by the depositor on enclosed separate
sheet.

(Please mark what applies)

P.T.O.

FISH & NEAVE

875 THIRD AVENUE
NEW YORK, N.Y. 10022-6250

TELEPHONE (212) 715-0600

TELEX 14-8367

CABLE ADDRESS: FISHNEAVE

TELECOPIER (212) 715-0674

October 16, 1991

CHARLES S. SMITH
DAVID W. PLANT
ALBERT E. PEY
JOHN D. THOMPSON
HERBERT F. SCHWARTZ
LARRY I. GULLBERG
WILLIAM J. SILBERT
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DAVID J. LEE
PATRICIA A. MARTONE

JAMES F. HALEY, JR.
RICHARD W. BARNES
LAURENCE S. ROGERS
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VINCENT W. BALLADINO
ROBERT J. GOLDMAN
THOMAS L. SECREST
DANIEL B. BARTY
NORMAN H. BEAMES
KEVIN J. CULLMAN
ALEXANDER D. DUTCHER
BARBARA PROSOPY
BARBARA A. PIERCE
ROS E. SHULMAN
DOUGLAS J. SILBERT
DENISE L. LORING
JEFFREY L. INGBERMAN

FREDERICK P. FISH
1959-1930
CHARLES NEAVE
1967-1937

A. PETER ABLE
RICHARD A. HUI

THOMAS J. VETTER

C. JOSEPH LANGRISH, II
LISA E. CRISTAL
EDWARD P. KELLY
NORMAN S. BLOOMBERG
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DAVID C. PLACHE
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LORETTA A. WADSWORTH
ROBERT S. WILDES
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MARIE H. MCDONELL
WILLIAM A. SCHONEMAN

Deutsche Sammlung von Mikroorganismen
Und Zellkulturen GmbH
Mascheroder Weg 1b
D-3300 Braunschweig
Federal Republic of Germany

Biogen - B8/B8 CIP
Deposits DSM 1791-1793; 1851-1854

Dear Sir:

We have enclosed seven (7) applications to convert the above-identified deposits already deposited at the DSM into deposits under the Budapest Treaty. The DSM designations, as well as the strain designations given by the depositor, are identified on the application forms. In addition, we enclose copies of the "Acknowledgement of Receipt and Acceptance" forms for these deposits and the "Accession Form for Deposit" for DSM 1851-1854, containing the media and culture requirements. Please send your debit note for these conversions to my attention.

Please note that the original depositor has undergone a corporate name and address change from Biogen N.V., 24 Handelskad, Willemsted, Curacao, Netherlands, to Biogen, Inc., 14 Cambridge Center, Cambridge, Massachusetts, U.S.A. 02142. This name and address change has been duly registered according to the national laws in the Patent Office of each country where a patent application has been filed referencing these deposits.

If you have any questions or require further information, please do not hesitate to contact us.

Thanks for your help.

Yours very truly,

James F. Haley, Jr.
Ivor R. Elrifi
Attorneys for Biogen, Inc.

JFH/IRE:bb
Enclosures

RECOGNITION OF THE DEPOSIT OF MICROORGANISMS
FOR THE PURPOSE OF PATENT PROCEDURE

STATEMENT IN THE CASE OF AN ORIGINAL DEPOSIT
pursuant to Rule 6.1

To
DEUTSCHE SAMMLUNG VON MIKROORGANISMEN
UND ZELLKULTUREN GmbH
Mascheroder Weg 1b
D-3300 Braunschweig
Federal Republic of Germany

To be filled in by the Depository Authority

DSM-Accession number :

Date culture received :

BACTERIA/FUNGI¹

THE UNDERSIGNED HEREBY DEPOSITS UNDER THE BUDAPEST TREATY THE MICROORGANISM IDENTIFIED HEREUNDER AND UNDERTAKES NOT TO WITHDRAW THE DEPOSIT FOR THE PERIOD SPECIFIED IN RULE 9.1²

I. IDENTIFICATION OF THE MICROORGANISM

Identification reference³ :

HFIF-D
M5219 (G-pPLa-HFIF-67-12)

Taxonomic designation⁴ :

Escherichia coli

The culture to be deposited is :

(X) a pure culture

() a mixture of microorganisms

(Mark with a cross where applicable)

II. CONDITIONS FOR CULTIVATION

(X)⁵

Medium:

as according to original
deposit application for DSM 1851

pH before sterilisation :

Sterilisation min at °C

pH after sterilisation:

Oxygen relationship :

() aerobic

() microaerophilic

() obligate anaerobic

Specific gaseous requirements :

Incubation temperature: °C

Incubation time:

Short term storage at: °C

Interval of transfer:

¹ The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neu kombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

² This form may also be used if the undersigned converts into a deposit under the Budapest Treaty the deposit of a microorganism that he or his predecessor in title has already deposited, outside the Budapest Treaty, with the same depository institution either before (Rule 6.4(d)) or after the acquisition by that institution of the status of international depository authority.

³ Number, symbols etc., given to the microorganism by the depositor.

⁴ It is strongly recommended that the taxonomic designation and/or scientific description (see under VII.) of the microorganism be indicated.

⁵ Mark with a cross if additional information is given on an attached sheet.

III. CONDITIONS FOR LONG TERM STORAGE

(X)⁵

IV. CONDITIONS FOR TESTING VIABILITY

(X)⁵

V. COMPONENTS OF MIXED CULTURES (WHEN APPLICABLE)

(X)⁵

Description of components:

Method(s) for checking presence of components:

⁵ Mark with a cross if additional information is given on an attached sheet.

VI. PROPERTIES DANGEROUS TO HEALTH OR ENVIRONMENT

Hazard group of the microorganisms, named under I., according to DIN 58 956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9:¹

.....

THE STRAIN HAS TO BE HANDLED UNDER THE FOLLOWING LABORATORY CONTAINMENT LEVEL¹:

☐ L1

☐ L2

☐ L3

☐ L4

IS THIS STRAIN DANGEROUS TO HEALTH OR THE ENVIRONMENT ?

☐ YES

☒ NO

(if yes, please specify:)

☒⁵

☒ the undersigned is not aware of such properties

IF THE MICROORGANISM IS GENETICALLY MANIPULATED:

1. PLEASE INDICATE ALL THE RELEVANT GENETIC PROPERTIES:

general genetic recombination (rec):

sensitivities:

resistances:

modifications:

restrictions:

auxotrophies:

2. DESIGNATION OF THE DONOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE PLASMID:

3. If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKBS guidelines⁶ or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION).

1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINITELY HAVE NO PATHOGENIC POTENTIAL.

☐ YES

2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL.

☐ YES

IN THE LATTER CASE PLEASE NOTE:

According to the regulations of the ZKBS⁶ the DSM can only accept genetically manipulated, potentially pathogenic organisms for deposition when a copy of the permit issued by the ZKBS⁶ (or by an equivalent national biological safety commission) for work on the organisms accompanies the deposition form

¹ The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neu kombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

⁵ Mark with a cross if additional information is given on an attached sheet.

⁶ ZKBS = Zentrale Kommission für Biologische Sicherheit (Central Commission for Biological Safety)

VII. SCIENTIFIC DESCRIPTION⁷(x)⁵

VIII. ADDITIONAL DATA

()⁸IX. DEPOSITOR⁹

Name: Biogen, Inc.

Signature:

James F. Haley, Jr.
Ivor R. Elrifi
Attorneys for Biogen, Inc.

Address: 14 Cambridge Center
Cambridge, Massachusetts
02142

Date:

Fish & Neave
875 Third Avenue
New York, New York 10022

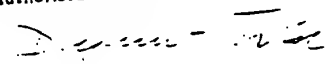
12/13/91

- ⁵ Mark with a cross if additional information is given on an attached sheet.
⁷ It is strongly recommended that the scientific description and/or proposed taxonomic designation (see 1.) of the microorganism be indicated.
⁸ Mark with a cross if additional information (other than the information referred to in footnote 4 is given on an attached sheet, such as the source of the microorganism, the name(s) and the address(es) of any other depository institution(s) with which the microorganism has been deposited, or the criterion used when drafting the proposed taxonomic designation (The supplying of such information is optional).
⁹ The name of the depositor must be identical with the signature.
In case of a legal entity the signatures of two representatives, officially nominated by this entity, are required.
Where the signature is required on behalf of a legal entity, the typewritten name(s) of the natural person(s) signing on behalf of the legal entity should accompany the signature(s).

INTERNATIONAL FORM

Biogen Inc.
14, Cambridge Center
Cambridge
Massachusetts
USA 02142

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT
issued pursuant to Rule 7.1 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

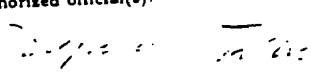
I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference given by the DEPOSITOR HFIF-D M5219 (G-pPLa-HFIF-67-12)	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY. DSM 1851
II. SCIENTIFIC DESCRIPTION AND/OR TAXONOMIC DESIGNATION	
The microorganism identified under I. above was accompanied by:	
<input type="checkbox"/> a scientific description <input checked="" type="checkbox"/> a proposed taxonomic designation	
(Mark with a cross where applicable)	
III. RECEIPT AND ACCEPTANCE	
This International Depositary Authority accepts this microorganism identified under I. above, which was received by it on 1981-10-01 (Date of original deposit) ¹	
IV. RECEIPT OF REQUEST FOR CONVERSION	
The microorganism identified under I above was received by this International Depositary Authority on 1980-06-05 (date of original deposit) and a request to convert the original deposit to a deposit under the Budapest Treaty was received by it on 1991-10-24 (date of receipt of request for conversion).	
V. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSM-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Address: Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):  Date: 1991-10-28

¹ Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired
Form DSM-BP/4 (sole page) 0291

INTERNATIONAL FORM

Biogen Inc.
14, Cambridge Center
Cambridge
Massachusetts
USA 02142

VIABILITY STATEMENT
issued pursuant to Rule 10.2 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

I. DEPOSITOR		II. IDENTIFICATION OF THE MICROORGANISM	
Name: Biogen Inc. Address: 14, Cambridge Center Cambridge Massachusetts USA 02142		Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY DSM 1851 Date of the deposit or of the transfer ¹ : 1981-10-01	
III. VIABILITY STATEMENT			
The viability of the microorganism identified under II above was tested on 1990-11-29 ² On that date, the said microorganism was (X) ³ viable () ³ no longer viable			
IV. CONDITIONS UNDER WHICH THE VIABILITY TEST HAS BEEN PERFORMED ⁴			
IV. INTERNATIONAL DEPOSITARY AUTHORITY			
Name: DSM DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Address: Mascheroder Weg 1 B D-3300 Braunschweig		Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):  Date: 1991-10-28	

- ¹ Indicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date (date of the new deposit or date of the transfer).
- ² In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.
- ³ Mark with a cross the applicable box.
- ⁴ Fill in if the information has been requested and if the results of the test were negative.

ACKNOWLEDGEMENT OF RECEIPT AND ACCEPTANCE

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikroorganismen.

Name and address
of depositor:

BIOGEN N.V.
24 Handelskad
Willemsted,
Curacao, Netherland Antilles

Identification reference of
the microorganism used by
the depositor:

HFIF-E
K12ΔHI (G-pPLa-HFIF-67-12)

Taxonomic designation of
the microorganism provi-
ded by the depositor:

Escherichia coli

DSM accession number of
the microorganism;

DSM 1852

Date of receipt of the
viable microorganism:

June 5, 1980

In addition to the identification reference and the taxonomic designation the depositor^{XXX}
~~has provided~~ / has not provided a scientific description of the microorganism.

- ☒ The microorganism has been sent to the DSM directly by the depositor.
☐ The microorganism has been sent to the DSM on behalf of the depositor by the following
depository under the designation and accession number given: —

As stated by the depositor the microorganism may be rendered accessible to any third party
under the following conditions:

- ☐ without any restrictions
☒ according to Rule 28 EPC and to the agreement between the European Patent Organisation
and the DSM (Official Journal EPD 5, 301-307, 1978) and/or
☒ according to the Swedish patent legislation and to the agreement between the Swedish
Patent Office and the DSM (Svensk Patenttidning nr 12, 1979)
☒ in accordance with the "Declaration of Release" to be filed by the depositor with the
DSM and the German Patent Office (at present Form P 2570)
in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14)
and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of
☒ America and b) without any restriction on availability to the public of the culture
upon granting of a United States patent wherein the deposited microorganism is part
of the disclosure of the invention
☒ in accordance with the French patent law
☐ in accordance with the conditions as specified by the depositor on enclosed separate
sheet.

Göttingen, June 5, 1980

Place date DEUTSCHE SAMMLUNG VON MIKROORGANISMEN Signature
der
Gesellschaft für Biotechnologische Forschung mbH
Grisebachstrasse 8
D-3400 Göttingen

Gesellschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig, Tel.: (05 31) 70 08-1, Telex: 9-5 26 67

Vorsitzender des Aufsichtsrats:
Min. Dir. Dr. Friedrich Bischoff

Geschäftsführer:
Dr. Maria-Regina Kula
Dr. Helmut Zenträger

Bankkonto:
Gebr. Löffbecke, Braunschweig
Konto 23 781 (BLZ 270 305 00)

Registergericht:
Amtsgericht Braunschweig
HRB 477

ACCESSION FORM for
deposition of patent microorganisms

DSM accession number: DSM 1852
Date culture received: 5.11.79

The microorganism mentioned below is to be deposited with the DSM on account of
a patent application (to be) filed with

The deposit is made in accordance with Rule 28 EPC / with the Swedish patent legislation
(delete, if not applicable)

Name and address of depositor: BIOGEN N.V.
24 Handelskad
Willemsted
Curacao, Netherland Antilles

Identification reference of the
microorganism given by the depo-
sitor (strain number, symbols etc.):

HFIF - E

K12ΔHI (G-pLα - HFIF - 67-12)

Taxonomic designation of the
microorganism:

E. coli

A scientific description of the microorganism is attached on a separate sheet:

YES ☐

NO ☒

The microorganism to be deposited is

a pure culture

YES ☒

NO ☐

a mixture of strains :

YES ☐

NO ☒

In case of a mixed culture, please give a concise description on a separate sheet about the
components and methods to determine their viability.

Does the microorganism and/or its metabolic products present any hazard for man, animals,
plants or the environment: (if any, please specify on a separate sheet):

YES ☐

NO ☒

- ☒ The microorganism will be ^{hand delivered} ~~sent~~ to the DSM directly by the depositor.
☐ The microorganism will be sent to the DSM on behalf of the depositor by
the following depository under the designation and accession number given:

The microorganism may be rendered accessible after receipt and deposition to any third party

☐ without any restriction

☒ according to Rule 28 EPC and to the agreement between the European Patent Organisation
and the DSM (Official Journal EPO 3, 301-307, 1978) and/or

☒ according to the Swedish patent legislation and to the agreement between the Swedish
Patent Office and the DSM (Svensk Patenttidsning nr 12, 1979)

☒ in accordance with the "Declaration of Release" to be filed by the depositor with the
DSM and the German Patent Office (at present Form 2750)

☒ in accordance with a) Title 37, Code of Federal Regulations, Section 1.14 (37.CFR 1.14)
and Title 35, United States Code section 122 (35 U.S.C. 122) of the United States of
America and b) without any restrictions on the availability to the public of the culture
upon granting of the United States patent wherein the deposited microorganism is part
of the disclosure of the invention

☒ in accordance with the French patent law

☐ in accordance with the conditions as specified by the depositor on enclosed separate
sheet.

(Please mark what applies)

001-1077

P.T.O.

FISH & NEAVE

'875 THIRD AVENUE
NEW YORK, N.Y. 10022-6250

TELEPHONE: (212) 715-0800
TELEX 14-8367
CABLE ADDRESS: FISHNEAVE
TELECOPIER: (212) 715-0874

October 16, 1991

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JOHN D. THOMAS
HERBERT F. SCHWARTZ
LARS I. KULLERED
WILLIAM J. BILBREY
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WILLIAM A. SCHNEIDERMAN

Deutsche Sammlung von Mikroorganismen
Und Zellkulturen GmbH
Mascheroder Weg 1b
D-3300 Braunschweig
Federal Republic of Germany

Biogen - B8/B8 CIP
Deposits DSM 1791-1793; 1851-1854

Dear Sir:

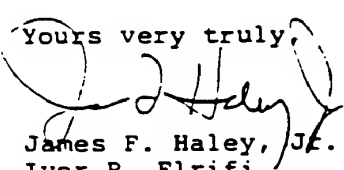
We have enclosed seven (7) applications to convert the above-identified deposits already deposited at the DSM into deposits under the Budapest Treaty. The DSM designations, as well as the strain designations given by the depositor, are identified on the application forms. In addition, we enclose copies of the "Acknowledgement of Receipt and Acceptance" forms for these deposits and the "Accession Form for Deposit" for DSM 1851-1854, containing the media and culture requirements. Please send your debit note for these conversions to my attention.

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If you have any questions or require further information, please do not hesitate to contact us.

Thanks for your help.

Yours very truly,


James F. Haley, Jr.
Ivor R. Elrifi
Attorneys for Biogen, Inc.

JFH/IRE:bb
Enclosures

RECOGNITION OF THE DEPOSIT OF MICROORGA 5
FOR THE PURPOSE OF PATENT PROCEDURE

STATEMENT IN THE CASE OF AN ORIGINAL DEPOSIT
pursuant to Rule 6.1

To
DEUTSCHE SAMMLUNG VON MIKROORGANISMEN
UND ZELLKULTUREN GmbH
Mascheroder Weg 1b
D-3300 Braunschweig
Federal Republic of Germany

To be filled in by the Depository Authority

DSM-Accession number :

Date culture received :

BACTERIA/FUNGI¹

THE UNDERSIGNED HEREBY DEPOSITS UNDER THE BUDAPEST TREATY THE MICROORGANISM IDENTIFIED HEREUNDER AND UNDERTAKES NOT TO WITHDRAW THE DEPOSIT FOR THE PERIOD SPECIFIED IN RULE 9.1²

I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference ³ : HFIF-E K12ΔHI (G-pPLa-HFIF-67-12) Taxonomic designation ⁴ : Escherichia coli	The culture to be deposited is : (X) a pure culture () a mixture of microorganisms (Mark with a cross where applicable)
II. CONDITIONS FOR CULTIVATION (X) ⁵	
Medium: as according to original deposit application for DSM 1852	pH before sterilisation : Sterilisation min at °C pH after sterilisation: Oxygen relationship : () aerobic () microaerophilic () obligate anaerobic Specific gaseous requirements : Incubation temperature: °C Incubation time: Short term storage at: °C Interval of transfer:

¹ The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neu kombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

² This form may also be used if the undersigned converts into a deposit under the Budapest Treaty the deposit of a microorganism that he or his predecessor in title has already deposited, outside the Budapest Treaty, with the same depository institution either before (Rule 6.4(d)) or after the acquisition by that institution of the status of international depository authority.

³ Number, symbols etc., given to the microorganism by the depositor.

⁴ It is strongly recommended that the taxonomic designation and/or scientific description (see under VII.) of the microorganism be indicated.

⁵ Mark with a cross if additional information is given on an attached sheet.

III. CONDITIONS FOR LONG TERM STORAGE

(X)⁵

IV. CONDITIONS FOR TESTING VIABILITY

(X)⁵

V. COMPONENTS OF MIXED CULTURES (WHEN APPLICABLE)

(X)⁵

Description of components:

Method(s) for checking presence of components:

⁵ Mark with a cross if additional information is given on an attached sheet.

VI. PROPERTIES DANGEROUS TO HEALTH OR ENVIRONMENT

Hazard group of the microorganisms, named under I. according to DIN 58 956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9:

THE STRAIN HAS TO BE HANDLED UNDER THE FOLLOWING LABORATORY CONTAINMENT LEVEL¹:

() L1

() L2

() L3

() L4

IS THIS STRAIN DANGEROUS TO HEALTH OR THE ENVIRONMENT ?

() YES

(X) NO

(if yes, please specify:)

(X)⁵

(X) the undersigned is not aware of such properties

IF THE MICROORGANISM IS GENETICALLY MANIPULATED:

1. PLEASE INDICATE ALL THE RELEVANT GENETIC PROPERTIES:

general genetic recombination (rec):

sensitivities:

resistances:

modifications:

restrictions:

auxotrophies:

2. DESIGNATION OF THE DONOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE PLASMID:

3. If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKBS guidelines⁶ or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION).

1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINITELY HAVE NO PATHOGENIC POTENTIAL.

() YES

2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL.

() YES

IN THE LATTER CASE PLEASE NOTE:

According to the regulations of the ZKBS⁶ the DSM can only accept genetically manipulated, potentially pathogenic organisms for deposition when a copy of the permit issued by the ZKBS⁶ (or by an equivalent national biological safety commission) for work on the organisms accompanies the deposition form

¹ The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro-neukombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

⁵ Mark with a cross if additional information is given on an attached sheet.

⁶ ZKBS = Zentrale Kommission für Biologische Sicherheit (Central Commission for Biological safety)

VII. SCIENTIFIC DESCRIPTION⁷(X)⁵

VIII. ADDITIONAL DATA

()⁸IX. DEPOSITOR⁹

Name: Biogen, Inc.

Signature:

James F. Haley, Jr.
James F. Haley, Jr.
Ivor R. Elrifi
Attorneys for Biogen, Inc.
Fish & Neave
875 Third Avenue
New York, New York 10022

Address: 14 Cambridge Center
Cambridge, Massachusetts
02142

Date:

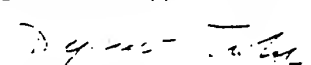
10/13/71

- ⁵ Mark with a cross if additional information is given on an attached sheet.
⁷ It is strongly recommended that the scientific description and/or proposed taxonomic designation (see I.) of the microorganism be indicated.
⁸ Mark with a cross if additional information (other than the information referred to in footnote 4 is given on an attached sheet, such as the source of the microorganism, the name(s) and the address(es) of any other depository institution(s) with which the microorganism has been deposited, or the criterion used when drafting the proposed taxonomic designation (The supplying of such information is optional).
⁹ The name of the depositor must be identical with the signature.
In case of a legal entity the signatures of two representatives, officially nominated by this entity, are required.
Where the signature is required on behalf of a legal entity, the typewritten name(s) of the natural person(s) signing on behalf of the legal entity should accompany the signature(s).

INTERNATIONAL FORM

Biogen Inc.
14, Cambridge Center
Cambridge
Massachusetts
USA 02142

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT
issued pursuant to Rule 7.1 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

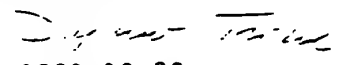
I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference given by the DEPOSITOR HFIF-E K12 Δ HI (G-pPLa-HFIF-67-12)	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY DSM 1852
II. SCIENTIFIC DESCRIPTION AND/OR TAXONOMIC DESIGNATION	
The microorganism identified under I. above was accompanied by: <div style="margin-left: 40px;"> <input type="checkbox"/> a scientific description <input checked="" type="checkbox"/> a proposed taxonomic designation </div> (Mark with a cross where applicable)	
III. RECEIPT AND ACCEPTANCE	
This International Depositary Authority accepts this microorganism identified under I. above, which was received by it on 1981-10-01 (Date of original deposit) ¹	
IV. RECEIPT OF REQUEST FOR CONVERSION	
The microorganism identified under I above was received by this International Depositary Authority on 1980-06-05 (date of original deposit) and a request to convert the original deposit to a deposit under the Budapest Treaty was received by it on 1991-10-24 (date of receipt of request for conversion).	
V. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSM-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Address: Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):  Date: 1991-10-28

¹ Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired

INTERNATIONAL FORM

Biogen Inc.
14, Cambridge Center
Cambridge
Massachusetts
USA 02142

VIABILITY STATEMENT
issued pursuant to Rule 10.2 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

I. DEPOSITOR	II. IDENTIFICATION OF THE MICROORGANISM
Name: Biogen Inc. 14, Cambridge Center Address: Cambridge Massachusetts USA 02142	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 1852 Date of the deposit or of the transfer ¹ : 1981-10-01
III. VIABILITY STATEMENT	
The viability of the microorganism identified under II above was tested on 1990-11-29 ² On that date, the said microorganism was (X) ³ viable () ³ no longer viable	
IV. CONDITIONS UNDER WHICH THE VIABILITY TEST HAS BEEN PERFORMED ⁴	
IV. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSM DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Address: Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):  Date: 1991-10-28

¹ Indicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date (date of the new deposit or date of the transfer).

² In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.

³ Mark with a cross the applicable box.

⁴ Fill in if the information has been requested and if the results of the test were negative.

GESELLSCHAFT FÜR BIOTECHNOLOGISCHE FORSCHUNG MBH

DSM · Grisebachstrasse 8 · D-3400 Göttingen, Germany

Tel. (05 51) 39 38 22 / 39 38 23

ACKNOWLEDGEMENT OF RECEIPT AND ACCEPTANCE

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikroorganismen.

Name and address
of depositor:

BIOGEN N.V.
24 Handelskad
Willemsted,
Curacao, Netherland Antilles

Identification reference of
the microorganism used by
the depositor:

HFIF-F
M5219 (G-pPLa -HFIF-67-12A19)

Taxonomic designation of
the microorganism provided
by the depositor:

Escherichia coli

DSM accession number of
the microorganism:

DSM 1853

Date of receipt of the
viable microorganism:

June 5, 1980

In addition to the identification reference and the taxonomic designation the depositor ~~has~~ provided / has not provided a scientific description of the microorganism.

- ☒ The microorganism has been sent to the DSM directly by the depositor.
☐ The microorganism has been sent to the DSM on behalf of the depositor by the following depository under the designation and accession number given:

As stated by the depositor the microorganism may be rendered accessible to any third party under the following conditions:

- ☐ without any restrictions
☒ according to Rule 28 EPC and to the agreement between the European Patent Organisation and the DSM (Official Journal EPO 5, 301-307, 1978) and/or
☒ according to the Swedish patent legislation and to the agreement between the Swedish Patent Office and the DSM (Svensk Patenttidning nr 12, 1979)
☒ in accordance with the "Declaration of Release" to be filed by the depositor with the DSM and the German Patent Office (at present Form P 2570)
☒ in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14) and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of America and b) without any restriction on availability to the public of the culture upon granting of a United States patent wherein the deposited microorganism is part of the disclosure of the invention
☒ in accordance with the French patent law
☐ in accordance with the conditions as specified by the depositor on enclosed separate sheet.

Göttingen, June 5, 1980

Place date DEUTSCHE SAMMLUNG VON MIKROORGANISMEN Signature
 der
 Gesellschaft für Biotechnologische Forschung mbH
 Grisebachstrasse 8
 D-3400 Göttingen

Gesellschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig, Tel.: (05 31) 70 08-1, Telex: 9-5 26 87

Vorsitzender des Aufsichtsrats:
Min. Dr. Dr. Friedrich Bischoff

Geschäftsführer:
Dr. Maria-Regina Kula
Dr. Helmut Zeitträger

Bankkonto:
Gebr. Lohbecke, Braunschweig
Konto 23 781 (BLZ 270 305 00)

Registriergericht:
Amtsgericht Braunschweig
HRB 477

003-0979

ACCESSION FORM for
deposition of patent microorganisms

DSM accession number: DSM 1353
Date culture received: 5 June 1982

The microorganism mentioned below is to be deposited with the DSM on account of
a patent application (to be) filed with

The deposit is made in accordance with Rule 28 EPC / with the Swedish patent legislation
(delete, if not applicable)

Name and address of depositor:

BIOGEN N.V.
24 Handelskad
Willemsted
Curacao, Netherland Antilles

Identification reference of the
microorganism given by the depo-
sitor (strain number, symbols etc.):

HFIF - F
M5219 (G-pPLa - HFIF-67-12 Δ19)

Taxonomic designation of the
microorganism:

A scientific description of the microorganism is attached on a separate sheet:

YES ☐

NO ☒

The microorganism to be deposited is

a pure culture

YES ☒

NO ☐

a mixture of strains :

YES ☐

NO ☒

In case of a mixed culture, please give a concise description on a separate sheet about the
components and methods to determine their viability.

Does the microorganism and/or its metabolic products present any hazard for man, animals,
plants or the environment: (if any, please specify on a separate sheet):

YES ☐

NO ☒

☒ The microorganism will be ^{hand delivered} sent to the DSM directly by the depositor.

☐ The microorganism will be sent to the DSM on behalf of the depositor by
the following depository under the designation and accession number given:

The microorganism may be rendered accessible after receipt and deposition to any third party

☐ without any restriction

☒ according to Rule 28 EPC and to the agreement between the European Patent Organisation
and the DSM (Official Journal EPD 5, 301-307, 1978) and/or

☒ according to the Swedish patent legislation and to the agreement between the Swedish
Patent Office and the DSM (Svensk Patenttidning nr 12, 1979)

☒ in accordance with the "Declaration of Release" to be filed by the depositor with the
DSM and the German Patent Office (at present form 2750)

☒ in accordance with a) Title 37, Code of Federal Regulations, Section 1.14 (37.CFR 1.14)
and Title 35, United States Code section 122 (35 U.S.C. 122) of the United States of
America and b) without any restrictions on the availability to the public of the culture
upon granting of the United States patent wherein the deposited microorganism is part
of the disclosure of the invention

☒ in accordance with the French patent law

☐ in accordance with the conditions as specified by the depositor on enclosed separate
sheet.

(Please mark what applies)

P.T.O.

FISH & NEAVE

875 THIRD AVENUE
NEW YORK, N.Y. 10022-6250

TELEPHONE: (212) 715-0600

TELEX: 14-8387

CABLE ADDRESS: FISHNEAVE

TELECOPIER: (212) 715-0674

October 16, 1991

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LARRY I. KULLERED
WILLIAM J. GILBERT
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ROBERT A. JACKSON
JESSE J. JENNER
W. EDWARD BAILEY
DAVID J. LEE
PATRICIA A. HARTONE

JAMES F. HALEY, JR.
RICHARD H. BARNES
LAURENCE S. ROGERS
THOMAS L. BARNETT
VINCENT H. PALLADINO
ROBERT J. GOLDMAN
THOMAS L. DECREST
DANIEL W. BARTY
RODMAN H. BEANER
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BARBARA A. PIERCE
RON E. SHULMAN
DOUGLAS J. SILBERT
DENISE L. LORING
JEFFREY H. HUBERMAN

FREDERICK P. FISH
1895-1830
CHARLES NEAVE
1887-1937

A. PETERABLES
RICHARD A. HILL

THOMAS J. VETTER

C. JOSEPH LAMMON, II
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EDWARD P. GELLY
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JOHN R. DEMARIS
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LESLIE A. MEDDILL
CHRISTOPHER P. BOGIELLA

CHRISTINA MACRETT
KAREN T. JUDLOWE
GERARDO A. DELBOS
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JOHN W. MATTHEWS
NICOLA A. PRANO
DONALD A. REEVE
GABRIELLE E. HIGGINS
JENNIFER R. HALL
DONALD L. HODGINS
ELIZABETH M. ALDRIDGE
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JEFFREY R. HERN
LIANNA C. SALAS
BRADFORD L. FRIEDMAN
DEBRA A. BOWEN
LORETTA A. HIGGINS
MOREY S. WILSON
CHRISTOPHER J. HARNETT
MARIE H. HARNETT
WILLIAM A. SCHWARTZ

Deutsche Sammlung von Mikroorganismen
Und Zellkulturen GmbH
Mascheroder Weg 1b
D-3300 Braunschweig
Federal Republic of Germany

Biogen - B8/B8 CIP
Deposits DSM 1791-1793; 1851-1854

Dear Sir:

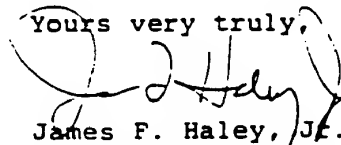
We have enclosed seven (7) applications to convert the above-identified deposits already deposited at the DSM into deposits under the Budapest Treaty. The DSM designations, as well as the strain designations given by the depositor, are identified on the application forms. In addition, we enclose copies of the "Acknowledgement of Receipt and Acceptance" forms for these deposits and the "Accession Form for Deposit" for DSM 1851-1854, containing the media and culture requirements. Please send your debit note for these conversions to my attention.

Please note that the original depositor has undergone a corporate name and address change from Biogen N.V., 24 Handelskad, Willemsted, Curacao, Netherland Antilles, to Biogen, Inc., 14 Cambridge Center, Cambridge, Massachusetts, U.S.A. 02142. This name and address change has been duly registered according to the national laws in the Patent Office of each country where a patent application has been filed referencing these deposits.

If you have any questions or require further information, please do not hesitate to contact us.

Thanks for your help.

Yours very truly,



James F. Haley, Jr.
Ivor R. Elrifi
Attorneys for Biogen, Inc.

JFH/IRE:bb
Enclosures

BUDAPEST TREATY ON THE INTERNATIONAL
RECOGNITION OF THE DEPOSIT OF MICROORGANISMS
FOR THE PURPOSE OF PATENT PROCEDURE

STATEMENT IN THE CASE OF AN ORIGINAL DEPOSIT
pursuant to Rule 6.1

To
DEUTSCHE SAMMLUNG VON MIKROORGANISMEN
UND ZELLKULTUREN GmbH
Mascheroder Weg 1b
D-3300 Braunschweig
Federal Republic of Germany

To be filled in by the Depository Authority

DSM-Accession number :

Date culture received :

BACTERIA/FUNGI¹

THE UNDERSIGNED HEREBY DEPOSITS UNDER THE BUDAPEST TREATY THE MICROORGANISM IDENTIFIED HEREUNDER AND
UNDERTAKES NOT TO WITHDRAW THE DEPOSIT FOR THE PERIOD SPECIFIED IN RULE 9.1²

I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference ³ : HFIF-F M5219 (G-pPLa-HFIF-67-12Δ19) Taxonomic designation ⁴ : Escherichia coli	The culture to be deposited is : (X) a pure culture () a mixture of microorganisms (Mark with a cross where applicable)
II. CONDITIONS FOR CULTIVATION (X) ⁵	
Medium: as according to original deposit application DSM 1853	pH before sterilisation : Sterilisation min at °C pH after sterilisation: Oxygen relationship : () aerobic () microaerophilic () obligate anaerobic Specific gaseous requirements : Incubation temperature: °C Incubation time: Short term storage at: °C Interval of transfer:

¹ The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neu kombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

² This form may also be used if the undersigned converts into a deposit under the Budapest Treaty the deposit of a microorganism that he or his predecessor in title has already deposited, outside the Budapest Treaty, with the same depository institution either before (Rule 6.4(d)) or after the acquisition by that institution of the status of international depository authority.

³ Number, symbols etc., given to the microorganism by the depositor.

⁴ It is strongly recommended that the taxonomic designation and/or scientific description (see under VII.) of the microorganism be indicated.

⁵ Mark with a cross if additional information is given on an attached sheet.

III. CONDITIONS FOR LONG TERM STORAGE

(X)⁵

IV. CONDITIONS FOR TESTING VIABILITY

(X)⁵

V. COMPONENTS OF MIXED CULTURES (WHEN APPLICABLE)

(X)⁵

Description of components:

Method(s) for checking presence of components:

⁵ Mark with a cross if additional information is given on an attached sheet.

VI. PROPERTIES DANGEROUS TO HEALTH OR ENVIRONMENT¹

Hazard group of the microorganisms named under I. according to DIN 58 956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9:¹

THE STRAIN HAS TO BE HANDLED UNDER THE FOLLOWING LABORATORY CONTAINMENT LEVEL¹:

- () L1 () L2
() L3 () L4

IS THIS STRAIN DANGEROUS TO HEALTH OR THE ENVIRONMENT ? () YES (X) NO
(if yes, please specify:) (X)⁵

(X) the undersigned is not aware of such properties

IF THE MICROORGANISM IS GENETICALLY MANIPULATED:

1. PLEASE INDICATE ALL THE RELEVANT GENETIC PROPERTIES:

general genetic recombination (rec):

sensitivities:

resistances:

modifications:

restrictions:

auxotrophies:

2. DESIGNATION OF THE DONOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE PLASMID:

3. If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKBS guidelines⁶ or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION).

1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINITELY HAVE NO PATHOGENIC POTENTIAL.

() YES

2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL.

() YES

IN THE LATTER CASE PLEASE NOTE:

According to the regulations of the ZKBS⁶ the DSM can only accept genetically manipulated, potentially pathogenic organisms for deposition when a copy of the permit issued by the ZKBS⁶ (or by an equivalent national biological safety commission) for work on the organisms accompanies the deposition form

¹ The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

⁵ Mark with a cross if additional information is given on an attached sheet.

⁶ ZKBS = Zentrale Kommission für Biologische Sicherheit (Central Commission for Biological safety)

VII. SCIENTIFIC DESCRIPTION⁷X)⁵

VIII. ADDITIONAL DATA

()⁸IX. DEPOSITOR⁹

Name: Biogen, Inc.

Signature:

James F. Haley, Jr.
Ivor R. Elrifi
Attorneys for Biogen, Inc.

Address: 14 Cambridge Center
Cambridge, Massachusetts
02142

Date: Fish & Neave
875 Third Avenue
New York, New York 10022

- ⁵ Mark with a cross if additional information is given on an attached sheet.
⁷ It is strongly recommended that the scientific description and/or proposed taxonomic designation (see 1.) of the microorganism be indicated.
⁸ Mark with a cross if additional information (other than the information referred to in footnote 4 is given on an attached sheet, such as the source of the microorganism, the name(s) and the address(es) of any other depositary institution(s) with which the microorganism has been deposited, or the criterion used when drafting the proposed taxonomic designation (The supplying of such information is optional).
⁹ The name of the depositor must be identical with the signature.
In case of a legal entity the signatures of two representatives, officially nominated by this entity, are required.
Where the signature is required on behalf of a legal entity, the typewritten name(s) of the natural person(s) signing on behalf of the legal entity should accompany the signature(s).

INTERNATIONAL FORM

Biogen Inc.
14, Cambridge Center
Cambridge
Massachusetts
USA 02142

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT
issued pursuant to Rule 7.1 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

I. IDENTIFICATION OF THE MICROORGANISM

Identification reference given by the DEPOSITOR

HFIF-F
M5219 (G-pPLa-HFIF-67-12A19)

Accession number given by the
INTERNATIONAL DEPOSITARY AUTHORITY

DSM 1853

II. SCIENTIFIC DESCRIPTION AND/OR TAXONOMIC DESIGNATION

The microorganism identified under I. above was accompanied by:

- () a scientific description
(X) a proposed taxonomic designation

(Mark with a cross where applicable)

III. RECEIPT AND ACCEPTANCE

This International Depositary Authority accepts this microorganism identified under I. above, which was received by it
on 1981-10-01 (Date of original deposit)¹

IV. RECEIPT OF REQUEST FOR CONVERSION

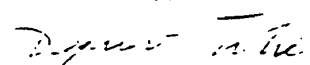
The microorganism identified under I above was received by this International Depositary Authority on 1980-06-05
(date of original deposit) and a request to convert the original deposit to a deposit under the Budapest Treaty was
received by it on 1991-10-24 (date of receipt of request for conversion).

V. INTERNATIONAL DEPOSITARY AUTHORITY

Name: DSM-DEUTSCHE SAMMLUNG VON
MIKROORGANISMEN UND ZELLKULTUREN GmbH

Address: Mascheroder Weg 1 B
D-3300 Braunschweig

Signature(s) of person(s) having the power
to represent the International Depositary Authority
or of authorised official(s):


Date: 1991-10-28

¹ Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired

INTERNATIONAL FORM

Biogen Inc.
14, Cambridge Center
Cambridge
Massachusetts
USA 02142

VIABILITY STATEMENT
issued pursuant to Rule 10.2 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

I. DEPOSITOR	II. IDENTIFICATION OF THE MICROORGANISM
Name: Biogen Inc. 14, Cambridge Center Address: Cambridge Massachusetts USA 02142	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 1853 Date of the deposit or of the transfer ¹ : 1981-10-01
III. VIABILITY STATEMENT	
The viability of the microorganism identified under II above was tested on 1990-11-29 ² On that date, the said microorganism was (X) ³ viable () ³ no longer viable	
IV. CONDITIONS UNDER WHICH THE VIABILITY TEST HAS BEEN PERFORMED ⁴	
IV. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSM DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Address: Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s): <i>Dieter Tiller</i> Date: 1991-10-28

¹ Indicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date (date of the new deposit or date of the transfer).

² In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.

³ Mark with a cross the applicable box.

⁴ Fill in if the information has been requested and if the results of the test were negative.

GESELLSCHAFT FÜR BIOTECHNOLOGISCHE FORSCHUNG MBH

DSM - Grisebachstrasse 8 - D-3400 Göttingen, Germany

Tel. (05 51) 39 38 22 / 39 38 23

ACKNOWLEDGEMENT OF RECEIPT AND ACCEPTANCE

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikroorganismen.

Name and address
of depositor:

BIOGEN N.V.
24 Handelskad
Willemsted,
Curacao, Netherland Antilles

Identification reference of
the microorganism used by
the depositor:

HFIF-G
M5219 (G-pPlc-HFIF-67-8)

Taxonomic designation of
the microorganism provi-
ded by the depositor:

Escherichia coli

DSM accession number of
the microorganism:

DSM 1854

Date of receipt of the
viable microorganism:

June 5, 1980

In addition to the identification reference and the taxonomic designation the depositor ~~has~~
~~XXXXXX~~ / has not provided a scientific description of the microorganism.

- ☒ The microorganism has been sent to the DSM directly by the depositor.
☐ The microorganism has been sent to the DSM on behalf of the depositor by the following
depository under the designation and accession number given:

As stated by the depositor the microorganism may be rendered accessible to any third party
under the following conditions:

- ☐ without any restrictions
☒ according to Rule 28 EPC and to the agreement between the European Patent Organisation
and the DSM (Official Journal EPO 5, 301-307, 1978) and/or
☒ according to the Swedish patent legislation and to the agreement between the Swedish
Patent Office and the DSM (Svensk Patenttidning nr 12, 1979)
☒ in accordance with the "Declaration of Release" to be filed by the depositor with the
DSM and the German Patent Office (at present Form P 2570)
in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14)
and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of
☒ America and b) without any restriction on availability to the public of the culture
upon granting of a United States patent wherein the deposited microorganism is part
of the disclosure of the invention
☒ in accordance with the French patent law
☐ in accordance with the conditions as specified by the depositor on enclosed separate
sheet.

Göttingen, June 5, 1980

Place date der Signatura
Gesellschaft für Biotechnologische Forschung mbH
Grisebachstrasse 8
D-3400 Göttingen

Gesellschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig, Tel.: (05 31) 70 06-1, Telex: 9-5 26 87

Vorsitzender des Aufsichtsrats:
Min. Dir. Dr. Friedrich Bischoff

Geschäftsführer:
Dr. Maria-Regina Kula
Dr. Helmut Zeitträger

Bankkonto:
Gebr. Lohbecke, Braunschweig
Konto 23 781 (BLZ 270 305 00)

Registriergericht:
Amtsgericht Braunschweig
HRB 477

003-0979

ACCESSION FORM for
deposition of patent microorganisms

DSM accession number: DSM 1354
Date culture received: 5 June 1979

The microorganism mentioned below is to be deposited with the DSM on account of
a patent application (to be) filed with

The deposit is made in accordance with Rule 28 EPC / with the Swedish patent legislation
(delete, if not applicable)

Name and address of depositor:

BIOGEN N.V.
24 Handelskad
Willemsted
Curacao, Netherland Antilles

Identification reference of the
microorganism given by the depo-
sitor (strain number, symbols etc.):

HFIF - G
M5219 (G - pPLc - HFIF - 67-8)

Taxonomic designation of the
microorganism:

E. coli

A scientific description of the microorganism is attached on a separate sheet:

YES ☐

NO ☒

The microorganism to be deposited is

a pure culture

YES ☒

NO ☐

a mixture of strains :

YES ☐

NO ☒

In case of a mixed culture, please give a concise description on a separate sheet about the
components and methods to determine their viability.

Does the microorganism and/or its metabolic products present any hazard for man, animals,
plants or the environment: (if any, please specify on a separate sheet):

YES ☐

NO ☒

☒ The microorganism will be ^{hand delivered} sent to the DSM directly by the depositor.

☐ The microorganism will be sent to the DSM on behalf of the depositor by
the following depository under the designation and accession number given:

The microorganism may be rendered accessible after receipt and deposition to any third party

☐ without any restriction

☒ according to Rule 28 EPC and to the agreement between the European Patent Organisation
and the DSM (Official Journal EPD 5, 301-307, 1978) and/or

☒ according to the Swedish patent legislation and to the agreement between the Swedish
Patent Office and the DSM (Svensk Patenttidsning nr 12, 1979)

☒ in accordance with the "Declaration of Release" to be filed by the depositor with the
DSM and the German Patent Office (at present Form 2750)

☒ in accordance with a) Title 37, Code of Federal Regulations, Section 1.14 (37.CFR 1.14)
and Title 35, United States Code section 122 (35 U.S.C. 122) of the United States of
America and b) without any restrictions on the availability to the public of the culture
upon granting of the United States patent wherein the deposited microorganism is part
of the disclosure of the invention

☒ in accordance with the French patent law

☐ in accordance with the conditions as specified by the depositor on enclosed separate
sheet.

(Please mark what applies)

P.T.O.

FISH & NEAVE

875 THIRD AVENUE
NEW YORK, N.Y. 10022-6250

TELEPHONE: (212) 715-0600

TELEX: 14-8367

CABLE ADDRESS: FISHNEAVE

TELECOPIER: (212) 715-0674

October 16, 1991

CHARLES B. SMITH
DAVID W. PLANT
ALBERT E. FET
JOHN D. TRAMONTINI
HERBERT F. SCHWARTZ
LARS I. KALLEBERG
WILLIAM J. BILBROTH
ERIC C. FOSLOW
JOHN E. NATHAN
ROBERT C. MORRAN
HENRY H. HERMAN
EDWARD F. BULLOWHNE
ROBERT B. JACKSON
JESSE J. JENNER
W. EDWARD BAILEY
DAVID J. LEE
PATRICIA A. MARTONE

JAMES F. HALEY, JR.
RICHARD W. BARNES
LAURENCE S. ROGERS
THOMAS L. BARNETT
VINCENT M. PALLADINO
ROBERT J. GOLDMAN
THOMAS L. BECKETT
DANIEL M. BARTY
NORMAN H. BEARER
KEVIN J. CULLINAN
ALEXANDER DUTERMOY
SUSAN PROCTOR
BARBARA A. PIERRE
RON E. SHULMAN
DOUGLAS J. GILBERT
DENISE L. LOHMEYER
JEFFREY H. HOBBSMAN

FREDERICK P. FISH
1985-1930
CHARLES NEAVE
1967-1937

A. PETER ADLER
RICHARD A. HILL

THOMAS J. VETTER

C. JOSEPH LAUBMAN, II
LISA E. CRISTAL
EDWARD P. KELLY
NAREN BLOMBERG
ALAN D. SMITH
DAVID C. PLACHE
JAMES A. HARRARD
DANIEL-DAVID HOUH
MITCHELL P. BROOK
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NAREN D. ENGELMANN
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DAVID A. LOEWENSTEIN
JOHN J. CARBONMAN
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KELSEY, BIX
MARTA E. GROSS
JOHN R. HINTZ
JOHN R. STORELLA
WILLIAM J. HECAGE
JOHN R. DEBARRIS
VICKI B. VEEREN
LESLIE A. MEDONELL
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GERARD A. MELAS
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NICOLA A. PIERARD
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JENNIFER M. HALL
DONALD L. BROADS
ELIZABETH M. ALDRIDGE
CLAY WILSON
SHREYA J. PANICH
JEREMY LACK
JAMES P. BERNIN
DONALD A. BRADSHAW
JEFFREY M. BERNIN
LIANNA C. SALMAN
BRADFORD L. FRIEDMAN
DEBRA A. BONTENPO
LORETTA A. HIGGINS
ROBERT S. WILSON
CHRISTOPHER J. HARNETT
NAREN M. HARRISON
WILLIAM A. SCHNEIDERMAN

Deutsche Sammlung von Mikroorganismen
Und Zellkulturen GmbH
Mascheroder Weg 1b
D-3300 Braunschweig
Federal Republic of Germany

Biogen - B8/B8 CIP
Deposits DSM 1791-1793; 1851-1854

Dear Sir:

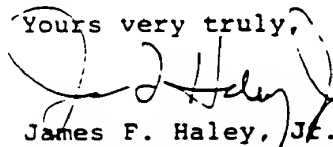
We have enclosed seven (7) applications to convert the above-identified deposits already deposited at the DSM into deposits under the Budapest Treaty. The DSM designations, as well as the strain designations given by the depositor, are identified on the application forms. In addition, we enclose copies of the "Acknowledgement of Receipt and Acceptance" forms for these deposits and the "Accession Form for Deposit" for DSM 1851-1854, containing the media and culture requirements. Please send your debit note for these conversions to my attention.

Please note that the original depositor has undergone a corporate name and address change from Biogen N.V., 24 Handelskad, Willemsted, Curacao, Netherland Antilles, to Biogen, Inc., 14 Cambridge Center, Cambridge, Massachusetts, U.S.A. 02142. This name and address change has been duly registered according to the national laws in the Patent Office of each country where a patent application has been filed referencing these deposits.

If you have any questions or require further information, please do not hesitate to contact us.

Thanks for your help.

Yours very truly,



James F. Haley, Jr.
Ivor R. Elrifi
Attorneys for Biogen, Inc.

JFH/IRE:bb
Enclosures

BUDAPEST TREATY ON THE INTERNATIONAL
RECOGNITION OF THE DEPOSIT OF MICROORGANISMS
FOR THE PURPOSE OF PATENT PROCEDURE

STATEMENT IN THE CASE OF AN ORIGINAL DEPOSIT
pursuant to Rule 6.1

To
DEUTSCHE SAMMLUNG VON MIKROORGANISMEN
UND ZELLKULTUREN GmbH
Mascheroder Weg 1b
D-3300 Braunschweig
Federal Republic of Germany

To be filled in by the Depositary Authority

DSM-Accession number :

Date culture received :

BACTERIA/FUNGI¹

THE UNDERSIGNED HEREBY DEPOSITS UNDER THE BUDAPEST TREATY THE MICROORGANISM IDENTIFIED HEREUNDER AND UNDERTAKES NOT TO WITHDRAW THE DEPOSIT FOR THE PERIOD SPECIFIED IN RULE 9.1²

I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference ³ : HFIF-G M5219 (G-pPLc-HFIF-67-8) Taxonomic designation ⁴ : Escherichia coli	The culture to be deposited is : (X) a pure culture () a mixture of microorganisms (Mark with a cross where applicable)
II. CONDITIONS FOR CULTIVATION (X) ⁵	
Medium: as according to original deposit application DSM 1854	pH before sterilisation : Sterilisation min at °C pH after sterilisation: Oxygen relationship : () aerobic () microaerophilic () obligate anaerobic Specific gaseous requirements : Incubation temperature: °C Incubation time: Short term storage at: °C Interval of transfer:

¹ The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neu kombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

² This form may also be used if the undersigned converts into a deposit under the Budapest Treaty the deposit of a microorganism that he or his predecessor in title has already deposited, outside the Budapest Treaty, with the same depositary institution either before (Rule 6.4(d)) or after the acquisition by that institution of the status of international depositary authority.

³ Number, symbols etc., given to the microorganism by the depositor.

⁴ It is strongly recommended that the taxonomic designation and/or scientific description (see under VII.) of the microorganism be indicated.

⁵ Mark with a cross if additional information is given on an attached sheet.

III. CONDITIONS FOR LONG TERM STORAGE

(X)⁵

IV. CONDITIONS FOR TESTING VIABILITY

(X)⁵

V. COMPONENTS OF MIXED CULTURES (WHEN APPLICABLE)

(X)⁵

Description of components:

Method(s) for checking presence of components:

⁵ Mark with a cross if additional information is given on an attached sheet.

VI. PROPERTIES DANGEROUS TO HEALTH OR ENVIRONMENT

Hazard group of the microorganisms, named under I. according to DIN 58 956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9:¹

.....

THE STRAIN HAS TO BE HANDLED UNDER THE FOLLOWING LABORATORY CONTAINMENT LEVEL¹:

() L1

() L2

() L3

() L4

IS THIS STRAIN DANGEROUS TO HEALTH OR THE ENVIRONMENT ?

() YES

(X) NO

(if yes, please specify:)

(X)⁵

(X) the undersigned is not aware of such properties

IF THE MICROORGANISM IS GENETICALLY MANIPULATED:

1. PLEASE INDICATE ALL THE RELEVANT GENETIC PROPERTIES:

general genetic recombination (rec):

sensitivities:

resistances:

modifications:

restrictions:

auxotrophies:

2. DESIGNATION OF THE DONOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE PLASMID:

3. If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKBS guidelines⁶ or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION).

1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINITELY HAVE NO PATHOGENIC POTENTIAL.

() YES

2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL.

() YES

IN THE LATTER CASE PLEASE NOTE:

According to the regulations of the ZKBS⁶ the DSM can only accept genetically manipulated, potentially pathogenic organisms for deposition when a copy of the permit issued by the ZKBS⁶ (or by an equivalent national biological safety commission) for work on the organisms accompanies the deposition form

¹ The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neu kombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

⁵ Mark with a cross if additional information is given on an attached sheet.

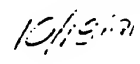
⁶ ZKBS = Zentrale Kommission für Biologische Sicherheit (Central Commission for Biological safety)

VII. SCIENTIFIC DESCRIPTION⁷(X)⁵

VIII. ADDITIONAL DATA

()⁶IX. DEPOSITOR⁹

Name: Biogen, Inc.

Signature: James F. Haley, Jr.
Ivor R. Elrifi
Attorneys for Biogen, Inc.Address: 14 Cambridge Center
Cambridge, Massachusetts
02142Date: Fish & Neave
875 Third Avenue
New York, New York 10022
⁵ Mark with a cross if additional information is given on an attached sheet.⁷ It is strongly recommended that the scientific description and/or proposed taxonomic designation (see 1.) of the microorganism be indicated.⁸ Mark with a cross if additional information (other than the information referred to in footnote 4 is given on an attached sheet, such as the source of the microorganism, the name(s) and the address(es) of any other depository institution(s) with which the microorganism has been deposited, or the criterion used when drafting the proposed taxonomic designation (The supplying of such information is optional).⁹ The name of the depositor must be identical with the signature.

In case of a legal entity the signatures of two representatives, officially nominated by this entity, are required.

Where the signature is required on behalf of a legal entity, the typewritten name(s) of the natural person(s) signing on behalf of the legal entity should accompany the signature(s).

INTERNATIONAL FORM

Biogen Inc.
14, Cambridge Center
Cambridge
Massachusetts
USA 02142

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT
issued pursuant to Rule 7.1 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

I. IDENTIFICATION OF THE MICROORGANISM

Identification reference given by the DEPOSITOR

HFIF-G

M5219 (G-pPlc-HFIF-67-8)

Accession number given by the
INTERNATIONAL DEPOSITARY AUTHORITY

DSM 1854

II. SCIENTIFIC DESCRIPTION AND/OR TAXONOMIC DESIGNATION

The microorganism identified under I. above was accompanied by:

- () a scientific description
(X) a proposed taxonomic designation

(Mark with a cross where applicable)

III. RECEIPT AND ACCEPTANCE

This International Depositary Authority accepts this microorganism identified under I. above, which was received by it
on 1981-10-01 (Date of original deposit)¹

IV. RECEIPT OF REQUEST FOR CONVERSION

The microorganism identified under I above was received by this International Depositary Authority on 1980-06-05
(date of original deposit) and a request to convert the original deposit to a deposit under the Budapest Treaty was
received by it on 1991-10-24 (date of receipt of request for conversion).

V. INTERNATIONAL DEPOSITARY AUTHORITY

Name: DSM-DEUTSCHE SAMMLUNG VON
MIKROORGANISMEN UND ZELLKULTUREN GmbH

Address: Mascheroder Weg 1 B
D-3300 Braunschweig

Signature(s) of person(s) having the power
to represent the International Depositary Authority
or of authorised official(s):

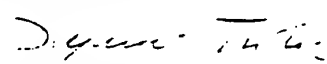
Date: 1991-10-28

¹ Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired

INTERNATIONAL FORM

Biogen Inc.
14, Cambridge Center
Cambridge
Massachusetts
USA 02142

VIABILITY STATEMENT
issued pursuant to Rule 10.2 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

I. DEPOSITOR	II. IDENTIFICATION OF THE MICROORGANISM
Name: Biogen Inc. 14, Cambridge Center Address: Cambridge Massachusetts USA 02142	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY DSM 1854 Date of the deposit or of the transfer ¹ : 1981-10-01
III. VIABILITY STATEMENT	
The viability of the microorganism identified under II above was tested on 1990-03-27 ² On that date, the said microorganism was (X) ³ viable () ³ no longer viable	
IV. CONDITIONS UNDER WHICH THE VIABILITY TEST HAS BEEN PERFORMED ⁴	
IV. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSM DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Address: Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):  Date: 1991-10-28

¹ Indicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date (date of the new deposit or date of the transfer).

² In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.

³ Mark with a cross the applicable box.

⁴ Fill in if the information has been requested and if the results of the test were negative.

DSM · Mascheroder Weg 1b · D-38124 Braunschweig

Fish & Neave
Attn. Ivor R. Elrifi
1251 Avenue of the Americas
New York, NY 10020
USA

Ihr Zeichen / Your ref.

Unser Zeichen / Our ref.

Tel.
05 31 / 26 16 -

Datum / Date

P 110 94/H

254

28.04.1994

Deposit DSM 1854 - Escherichia coli HFIF-G M5219 (G-pPLC-HFIF-67-8)

Dear Sirs,

we herewith confirm that the strain

Escherichia coli HFIF-G M5219 (G-pPLC-HFIF-67-8)

has been deposited at the DSM under the number DSM 1854 bearing the above mentioned identification reference. By a typographical error made in DSM the capital L in the designation G-pPLC-HFIF-67-8 has been misprinted as a small l. This is not correct. We regret this typographical mistake and send to you the newly filled in statements of receipt and acceptance in English and German stating the correct identification reference.

Yours faithfully,

DSM-Deutsche Sammlung von Mikro-
organismen und Zellkulturen GmbH

V. Weihs

Dr. Vera Weihs

RECEIVED

MAY - 2 1994

FISH & NEAVE - PATENT DEPT.
REFERRED TO IRE
ATED BY _____

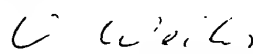
Note: The old incorrect forms may be destroyed.

BUDAPESTER VERTRAG ÜBER DIE INTERNATIONALE
ANERKENNUNG DER HINTERLEGUNG VON MIKROORGANISMEN
FÜR DIE ZWECKE VON PATENTVERFAHREN

INTERNATIONALES FORMBLATT

Biogen Inc.
14, Cambridge Center
Cambridge
Massachusetts
USA 02142

EMPFANGSBESTÄTIGUNG BEI ERSTHINTERLEGUNG,
ausgestellt gemäß Regel 7.1 von der unten angegebenen
INTERNATIONALEN HINTERLEGUNGSSTELLE

I. KENNZEICHNUNG DES MIKROORGANISMUS	
Vom HINTERLEGER zugeteiltes Bezugszeichen: HFIF-G M5219 (G-pPLc-HFIF-67-8)	Von der INTERNATIONALEN HINTERLEGUNGSSTELLE zugeteilte EINGANGSNUMMER: DSM 1854
II. WISSENSCHAFTLICHE BESCHREIBUNG UND/ODER VORGESCHLAGENE TAXONOMISCHE BEZEICHNUNG	
Mit dem unter I. bezeichneten Mikroorganismus wurde <input type="checkbox"/> eine wissenschaftliche Beschreibung <input checked="" type="checkbox"/> eine vorgeschlagene taxonomische Bezeichnung eingereicht. (Zutreffendes ankreuzen).	
III. EINGANG UND ANNAHME	
Diese internationale Hinterlegungsstelle nimmt den unter I bezeichneten Mikroorganismus an, der bei ihr am 1981-10-01 (Datum der Ersthinterlegung) ¹ eingegangen ist.	
IV. EINGANG DES ANTRAGS AUF UMWANDLUNG	
Der unter I bezeichnete Mikroorganismus ist bei dieser Internationalen Hinterlegungsstelle am 1980-06-05 eingegangen (Datum der Ersthinterlegung) und ein Antrag auf Umwandlung dieser Ersthinterlegung in eine Hinterlegung gemäß Budapest Vertrag ist am 1991-10-24 eingegangen (Datum des Eingangs des Antrags auf Umwandlung).	
V. INTERNATIONALE HINTERLEGUNGSSTELLE	
Name: DSM-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Anschrift: Mascheroder Weg 1b D-38124 Braunschweig	Unterschrift(en) der zur Vertretung der internationalen Hinterlegungsstelle befugten Person(en) oder des (der) von ihr ermächtigten Bediensteten:  Datum: 1994-04-28

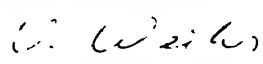
¹ Falls Regel 6.4 Buchstabe d zutrifft, ist dies der Zeitpunkt, zu dem der Status einer internationalen Hinterlegungsstelle erworben worden ist.

BUDAPEST TREATY ON THE INTERNAT. AL
RECOGNITION OF THE DEPOSIT OF MICROORGANISMS
FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

Biogen Inc.
14, Cambridge Center
Cambridge
Massachusetts
USA 02142

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT
issued pursuant to Rule 7.1 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference given by the DEPOSITOR: HFIF-G M5219 (G-pPLc-HFIF-67-8)	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 1854
II. SCIENTIFIC DESCRIPTION AND/OR PROPOSED TAXONOMIC DESIGNATION	
The microorganism identified under I. above was accompanied by: () a scientific description (X) a proposed taxonomic designation (Mark with a cross where applicable).	
III. RECEIPT AND ACCEPTANCE	
This International Depositary Authority accepts the microorganism identified under I. above, which was received by it on 1981-10-01 (Date of the original deposit) ¹ .	
IV. RECEIPT OF REQUEST FOR CONVERSION	
The microorganism identified under I above was received by this International Depositary Authority on 1980-06-05 (date of original deposit) and a request to convert the original deposit to a deposit under the Budapest Treaty was received by it on 1991-10-24 (date of receipt of request for conversion).	
V. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSM-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Address: Mascheroder Weg 1b D-38124 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):  Date: 1994-04-28

¹ Where Rule 6.4 (d) applies, such date is the date on which the status of international depositary authority was acquired.



BOARD OF TRUSTEES REPRESENTING

- AMERICAN ASSOCIATION OF IMMUNOLOGISTS
- AMERICAN INSTITUTE OF BIOLOGICAL SCIENCES
- AMERICAN PHYSIOLOGICAL SOCIETY
- AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS
- AMERICAN SOCIETY FOR MICROBIOLOGY
- AMERICAN SOCIETY OF PARASITOLOGISTS
- AMERICAN SOCIETY OF ZOOLOGISTS

- AMERICAN SOCIETY OF TROPICAL MEDICINE AND HYGIENE
- CLIMATE SOCIETY OF AMERICA
- INFECTIOUS DISEASES SOCIETY OF AMERICA
- NEUROLOGICAL SOCIETY OF AMERICA
- NATIONAL RESEARCH COUNCIL-NATIONAL ACADEMY OF SCIENCES
- SOCIETY OF PROTOZOOLOGISTS
- TRIBE CULTURE ASSOCIATION

• 301-881-2600

AMERICAN TYPE CULTURE COLLECTION

12301 PARKLAWN DRIVE
ROCKVILLE, MARYLAND 20852

February 27, 1981

James F. Haley, Jr., Esq.
Attorney for Biogen N.V.
c/o Fish & Neave
277 Park Avenue
New York, New York 10172

Gentlemen:

We received on February 26, 1981 a deposit of cultures of organisms identified as Escherichia coli M5219(G-pPLa-HFIF-67-124MI), HFIF-H, and Escherichia coli HB101(p[325]-qHFIF-4), HFIF-I.

These strains have been assigned the ATCC numbers 31824 and 31825, respectively.

We understand that these organisms are being deposited in the American Type Culture Collection (ATCC) in connection with the filing of an application for a patent.

We further understand that the deposit of these cultures does not grant to ATCC during the effective term of the patent anticipated a license, either expressed or implied to infringe the patent, and our release of these cultures to others does not grant them a license, either expressed or implied, to infringe the patent.

We further understand that if these cultures should die or be destroyed during the effective life of the patent it shall be your responsibility to replace them with living cultures of the same organisms.

We agree in consideration for a one-time service charge, not to distribute these cultures or any information relating thereto or to their deposits until such time as a patent has been issued disclosing the above deposits except in accordance with a U.S. Patent Office Rule of Practice, Rule 14, or until you authorize us to make these strains available. After a patent is issued and we are so informed the cultures will be made available for distribution to the public. The ATCC agrees to maintain the cultures for a period of 30 years from the deposit date. Non-payment of the service charge within 90 days of the deposit date relieves the ATCC from the above provisions.

Payment in the amount of \$1,140.00
received. Thank you.

Sincerely yours,

Bobbie A. Brandon

By: (Mrs.) Bobbie A. Brandon

An independent non-profit organization incorporated in Washington, D. C. and devoted to the
preservation of reference cultures and their distribution to the scientific community.

Date sheet to be completed by depositors to the
COLLECTION OF BACTERIA

31824

1. Scientific name of organism Escherichia coli MS219 (C-2012a-HFIF-67-126MT)
2. Strain designations other than ATCC number HFIF-H
3. Is this the type strain of this organism (see reverse side)? NO
4. If this strain has been designated in the literature as the type strain, please cite reference:

Do not write in this box	
ATCC #	<u>31824</u>
Accession date	<u>2/26/81</u>
Date received	<u>2/26/81</u>

5. Name and address of depositor: Biogen N.V.
15 Pietermaai
Curacao, Netherlands Antilles

6. Isolated by _____
from _____ date _____

7. If you did not isolate this strain, indicate from whom you received it:
ATCC — depositor —

8. Reason for deposit:
Requested by ATCC _____
Rev taxon: Species _____ Subspecies _____

Produces the antibiotic _____ Assay of _____
Production of _____ Other Patent

9. Maintenance:
Medium (attach formula) LB Broth or bactotryptone
Temperature 28°C Other LB Broth supplemented with 50 µg/ml Kanamycin

10. a) Does this organism survive: Freeze drying? Yes Freezing? Yes (poorly)
b) Recommended method for long-term preservation:
Freeze drying or LB Broth/glycerol or DMSO at -80°C
11. Is this strain zoopathogenic? NO If so, would you classify it as class 2, 3, or 4? _____
(see reverse side for description of classes)
12. Is this strain phytopathogenic? NO (Information required by Plant Quarantine Division, USDA)
If so, a) Is the geographical distribution of this organism general, limited, or unknown (encircle)?
b) Would you recommend that this strain be made available to any qualified investigator regardless of his location? _____
c) If not, what limits would you place on the distribution of this strain?

13. Please attach a complete description of this strain unless description is given in accompanying reprint.

14. References (Please enclose two (2) of each pertinent reprint, if available):

15. Comments:

Do not heat above 28°C.

ATCC Form 1-8 (1971)

J. J. H. J.
Signature of Depositor
Attorney for Biogen N.V.

AMERICAN TYPE CULTURE COLLECTION

12301 Parklawn Drive • Rockville, Maryland 20852 • 301 881 2600

Data sheet to be completed by depositors to the
COLLECTION OF BACTERIA

1. Scientific name of organism E. coli HB101 (D[325]-CHFIF-4)
2. Strain designations other than ATCC number HFIF-I
3. Is this the type strain of this organism (see reverse side)? No
4. If this strain has been designated in the literature as the type strain, please cite reference:

Do not write in this box	
ATCC #	<u>31825</u>
Accession date	<u>2/26/81</u>
Date received	<u>2/26/81</u>

5. Name and address of depositor: Biogen N.V.
15 Pietermaai
Curacao, Netherlands Antilles

6. Isolated by _____
from _____ date _____

7. If you did not isolate this strain, indicate from whom you received it: _____
ATCC — depositor —

8. Reason for deposit:
Requested by ATCC _____
New taxon: Species _____ Subspecies _____
Produces the antibiotic _____ Assay of _____
Production of _____ Other Patent

9. Maintenance:
Medium (attach formula) LB Broth or bactotryptone
Temperature _____ Other LB Broth supplemented with 100 µg/ml carbenic
lin and/or 10 µg/ml tetracycline;

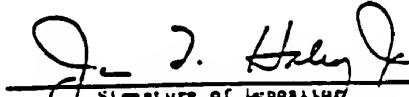
10. a) Does this organism survive: Freeze drying? Yes Freezing? Yes (poorly)
b) Recommended method for long-term preservation:
Freeze drying or LB Broth/glycerol or DMSO at -80°C
11. Is this strain zoonotic? No If so, would you classify it as class 2, 3, or 4? _____
(see reverse side for description of classes)
12. Is this strain phytopathogenic? No (Information required by Plant Quarantine Division, USDA)
If so, a) Is the geographical distribution of this organism general, limited, or unknown (encircle)?
b) Would you recommend that this strain be made available to any qualified investigator regardless of his location? _____
c) If not, what limits would you place on the distribution of this strain?

13. Please attach a complete description of this strain unless description is given in accompanying reprint.

14. References (Please enclose two (2) of each pertinent reprint, if available):

15. Comments:

ATCC Form 1-8 (1971)



Signature of Depositor
Attorney for Biogen N.V.

FISH & NEAVE

875 THIRD AVENUE
NEW YORK, N.Y. 10022-6250

TELEPHONE (212) 715-0800
TELEX 14-8367
CABLE ADDRESS FISHNEAVE
TELECOPIER (212) 715-0874

October 16, 1991

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WILLIAM J. DILBRETH
ERIC WOODLAW
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DENISE LORING
JEFFREY H. INDERMAN

FREDERICK R. FISH
1855-1930
CHARLES NEAVE
1867-1937

A. PETERADLER
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C. JOSEPH LAUDON
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EVAN BELL
JAMES P. BEEDIN
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LIAMAC SALAS
BRADFOOD, FRIEDMAN
DEBRA BONTEND
LORETTA M. HIRAGLIA
MORRIS HILDES
CHRISTOPHER J. HARNETT
MARIE M. HACHENOL
WILLIAM A. SCHONEMAN

Mrs. Bobbie Brandon
American Type Culture Collection
12301 Parklawn Drive
Rockville, MD 20852

Biogen - B8/B8 CIP
Deposits identified as ATCC 31824 and ATCC 31825

Dear Mrs. Brandon:

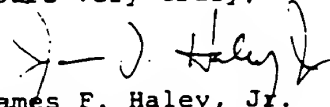
We have enclosed two (2) requests for conversion of the above-identified deposits to meet the requirements of the Budapest Treaty. The ATCC designations, as well as the strain designations given by the depositor, are identified on the request forms. In addition, we enclose copies of the letter of receipt of these deposits and of the original deposit applications containing the media and culture requirements.

Please note that the original depositor has undergone a corporate name and address change, from Biogen N.V., 15 Pietermaai, Curacao, Netherlands Antilles, to Biogen, Inc., 14 Cambridge Center, Cambridge, Massachusetts, U.S.A. 02142. This name and address change has been duly registered according to the national laws in the Patent Office of each country where a patent application has been filed referencing these deposits.

If you have any questions or require further information, please do not hesitate to contact us.

Thanks for your help.

Yours very truly,



James F. Haley, Jr.
Ivor R. Elrifi
Attorneys for Biogen, Inc.

JFH/IRE:bb
Enclosures



TO DEPOSIT OR TO CONVERT A DEPOSIT TO MEET THE REQUIREMENTS OF
BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE
DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

- *1. Name of deposit (microorganism, cell, seed, plasmid, etc.) Escherichia coli M5219
(G-pPLA-HFIF-67-12ΔMI) _____
2. Strain designation given by the depositor (number, symbols, etc.) HFIF-H _____
3. Is this an original deposit under the Budapest Treaty? _____
4. Is this a request for a conversion of a deposit already at the ATCC to meet the requirements of the Budapest Treaty? (If so, indicate ATCC designation.) Yes, ATCC 31824 _____
5. Is this deposit a mixture of microorganisms or cells? No _____
6. Details and conditions necessary for the cultivation of the strain, for its storage and for testing its viability and also, where a mixture of microorganisms is deposited, descriptions of the components of the mixture and at least one of the methods permitting the checking of their presence. _____
see attached sheets _____
7. An indication of the properties of the strain which are or may be dangerous to health or the environment, or an indication that the depositor is not aware of such properties. Depositor is not aware of any properties of the strain which are or may be dangerous to health or environment. _____
- *8. It is recommended that sufficient description be provided to allow the ATCC to confirm that the strain deposited generally conforms to that which the depositor states is being deposited (i.e., Gram negative rod). _____
- a. For cell culture deposits please complete. Is the cell being cultured in the presence of antibiotics (if so list the antibiotics) _____
- b. For hybridoma deposits please complete. What is the isotype of antibody produced? _____
- *9. Is this strain zoonotic? No _____ phytopathogenic? No _____
Yes _____
10. Does this strain contain plasmids relevant to the patent process? _____
If so, what physical containment level is required for experiments as described in the National Institutes of Health Guidelines involving Recombinant DNA Molecules (i.e., P1, P2, P3 and P4 facility)? P1 _____

*The answers to these questions are recommended but not required.

— FOR ATCC USE ONLY —	
ATCC DESIGNATION	_____
DATE CULTURE RECEIVED	_____
DATE VIABILITY TEST COMPLETED	_____



TO DEPOSIT OR TO CONVERT A DEPOSIT TO MEET THE REQUIREMENTS OF
BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE
DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

- *1. Name of deposit (microorganism, cell, seed, plasmid, etc.) Escherichia coli
HB101 (p[325]-qHFIF-4)
2. Strain designation given by the depositor (number, symbols, etc.) HFIF-I
3. Is this an original deposit under the Budapest Treaty? _____
4. Is this a request for a conversion of a deposit already at the ATCC to meet the requirements of the Budapest Treaty? (If so, indicate ATCC designation.) Yes, ATCC 31825
No
5. Is this deposit a mixture of microorganisms or cells? _____
6. Details and conditions necessary for the cultivation of the strain, for its storage and for testing its viability and also, where a mixture of microorganisms is deposited, descriptions of the components of the mixture and at least one of the methods permitting the checking of their presence. see attached sheets
7. An indication of the properties of the strain which are or may be dangerous to health or the environment, or an indication that the depositor is not aware of such properties. Depositor is not aware of any
properties of the strain which are or may be dangerous to health or
the environment.
- *8. It is recommended that sufficient description be provided to allow the ATCC to confirm that the strain deposited generally conforms to that which the depositor states is being deposited (i.e., Gram negative rod). _____
- a. For cell culture deposits please complete. Is the cell being cultured in the presence of antibiotics (if so list the antibiotics) _____
- b. For hybridoma deposits please complete. What is the isotype of antibody produced? _____
- *9. Is this strain zoopathogenic? No phytopathogenic? No
Yes
10. Does this strain contain plasmids relevant to the patent process? _____
If so, what physical containment level is required for experiments as described in the National Institutes of Health Guidelines involving Recombinant DNA Molecules (i.e., P1, P2, P3 and P4 facility)? P1

*The answers to these questions are recommended but not required.

— FOR ATCC USE ONLY —

ATCC DESIGNATION _____
DATE CULTURE RECEIVED _____
DATE VIABILITY TEST COMPLETED _____



BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF
THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3
AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2
To: (Name and Address of Depositor or Attorney)

James F. Haley, Jr., Ivor R. Elrifi
Fish & Neave
875 Third Avenue
New York, NY 10022

Deposited on Behalf of: Biogen, Inc. (Docket B8/B8 C 1P)

Identification Reference by Depositor:

ATCC Designation

Escherichia coli M5219 (G-pPLA-HFIF-67-12deltaMI), HFIF-H

31824

Escherichia coli HB101 (p[325]-qHFIF-4), HFIF-I

31825

The deposits were accompanied by: a scientific description X a proposed taxonomic description indicated above.

The deposits were received February 26, 1981 by this International Depository Authority and have been accepted. A request to convert the deposits to a deposit under the Budapest Treaty was received on October 23, 1991.

AT YOUR REQUEST:

X We will inform you of requests for the strains for 30 years.

The strains will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strains.

If the cultures should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace them with living cultures of the same.

The strains will be maintained for a period of at least 30 years after the date of deposit, and for a period of at least five years after the most recent request for a sample. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the cultures cited above was tested October 25, 1991. On that date, the cultures were viable.

International Depository Authority: American Type Culture Collection, Rockville, Md. 20852 USA

Signature of person having authority to represent ATCC:

Bobbie A. Brandon
Bobbie A. Brandon, Head, ATCC Patent Depository

Date: October 28, 1991



American Type Culture Collection

12301 Parklawn Drive • Rockville, MD 20852 USA • Telephone: (301)231-5520 Telex: 898-055 ATCCNORTH • FAX: 301-770-2587

BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3 AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2

To: (Name and Address of Depositor or Attorney)

James F. Haley, Jr., Ivor R. Elrifi
Fish & Neave
875 Third Avenue
New York, NY 10022

Deposited on Behalf of: Biogen, Inc. (Docket B8/B8 C 1P)

Identification Reference by Depositor:

ATCC Designation

Escherichia coli M5219 (G-pLa-HFIF-67-12ΔMI)
Escherichia coli HB101 (p[325]-gHFIF4)

31824
31825

The deposits were accompanied by: ☐ a scientific description ☒ a proposed taxonomic description indicated above.

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International Depository Authority: American Type Culture Collection, Rockville, Md. 20852 USA

Signature of person having authority to represent ATCC:

Bobbie A. Brandon
Bobbie A. Brandon, Head, ATCC Patent Depository

Date: May 6, 1994